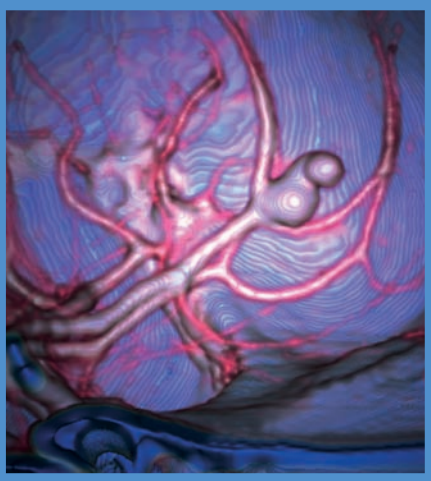
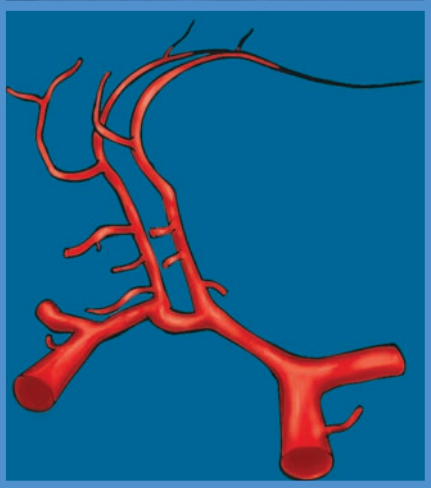
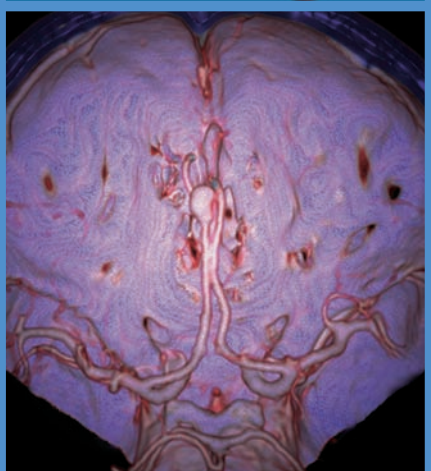






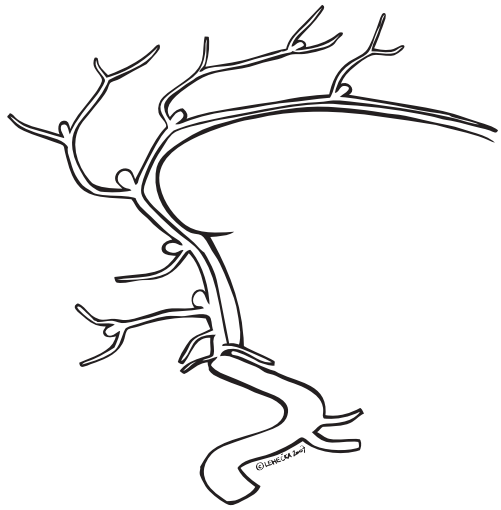
Distal Anterior Cerebral Artery Aneurysms

Martin Lehečka

University of Helsinki 2009

From the Department of Neurosurgery
Helsinki University Central Hospital
University of Helsinki
Helsinki, Finland

Distal Anterior Cerebral Artery Aneurysms



Martin Lehečka

Academic Dissertation

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Supervised by:

Professor **Juha Hernesniemi**, M.D., Ph.D.
Department of Neurosurgery
Helsinki University Central Hospital
Helsinki, Finland

Associate Professor **Mika Niemelä**, M.D., Ph.D.
Department of Neurosurgery
Helsinki University Central Hospital
Helsinki, Finland

Reviewed by:

Professor **Juha Öhman**, M.D., Ph.D.
Department on Neurosurgery
Tampere University Hospital
Tampere, Finland

Associate Professor **Timo Kumpulainen**, M.D., Ph.D.
Department of Neurosurgery
Oulu University Hospital
Oulu, Finland

To be discussed with:

Professor **Robert F. Spetzler**, M.D.
Director, Barrow Neurological Institute
J.N. Harber Chairman of Neurological Surgery
Professor, Section of Neurosurgery, University of Arizona
Phoenix, Arizona

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To my grandfather

Author's contact information:

Martin Lehečka
Department of Neurosurgery
Helsinki University Central Hospital
Topeliuksenkatu 5
00260 Helsinki
Finland
mobile: +358 50 427 2500
fax: +358 9 471 87560
e-mail: martin.lehecka@hus.fi

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Abstract

Objective: Distal anterior cerebral artery (DACA) aneurysms represent about 6% of all intracranial aneurysms. So far, only small series on treatment of these aneurysms have been published. Our aim is to evaluate the anatomic features, treatment results, and long-term outcome of DACA aneurysms. In addition, we address the current techniques for microneurosurgical treatment of these lesions.

Patients and methods: We analyzed the clinical and radiological data on 517 consecutive patients diagnosed with DACA aneurysm at two neurosurgical centers serving solely the Southern (Helsinki) and Eastern (Kuopio) Finland in 1936–2007. We used a defined subgroup of the whole study population in each part of the study. Detailed anatomic analysis was performed in 101 consecutive patients from 1998 to 2007. Treatment results were analyzed in 427 patients treated between 1980 to 2005, the era of CT imaging and microneurosurgery. With a median follow-up of 10 years we evaluated the long-term outcome of treatment in 280 patients with ruptured DACA aneurysm(s); no patients were lost to follow-up.

Results: DACA aneurysms, found most often (83%) at the A3 segment of the anterior cerebral artery (ACA), were smaller (median 6 mm vs. 8 mm), more frequently associated with multiple aneurysms (35% vs. 18%), and presented more often with intracerebral hematomas (ICHs) (53% vs. 26%) than ruptured aneurysms in general. They were associated with anomalies of the ACA in 23% of the patients. Microsurgical treatment showed similar complication rates (treatment morbidity 15%, treatment mortality 0.4%) as for other ruptured aneurysms. At one year after subarachnoid hemorrhage (SAH), DACA aneurysms had equally favorable outcome (GOS≥4) as other ruptured aneurysms (74% vs. 69%) but their mortality was lower (13% vs. 24%). Factors predicting unfavorable outcome for ruptured DACA aneurysms were advanced age, Hunt&Hess grade≥3, rebleeding before treatment, ICH, intraventricular hemorrhage, and severe preoperative hydrocephalus. The cumulative relative survival ratio showed 16% excess mortality in patients with ruptured DACA aneurysm during the first three years after SAH compared to the matched general population. From the fourth year onwards, there was no excess mortality during the follow-up. There were four episodes of recurrent SAH, only one due to treated DACA aneurysm, with a 10-year cumulative risk of 1.4%.

Conclusions: The special neurovascular features and frequent association with anterior cerebral artery anomalies must be taken into account when planning occlusive treatment of DACA aneurysms. With microneurosurgery, ruptured DACA aneurysms have equally favorable outcome but lower mortality at one year as ruptured aneurysms in general. Clipping of DACA aneurysms provides a long-lasting result, with very small rates of rebleeding. After surviving three years from rupture of DACA aneurysm, the long-term survival of these patients becomes similar to that of the matched general population.

Abbreviations

A1 = Proximal segment of anterior cerebral artery
A1A = Aneurysm of the A1 segment of anterior cerebral artery
A2 = A2 segment of anterior cerebral artery
A2A = Aneurysm of the A2 segment or frontobasal branch of anterior cerebral artery
A3 = A3 segment of anterior cerebral artery
A3A = Aneurysm of the A3 segment of anterior cerebral artery
A4 = A4 segment of anterior cerebral artery
A5 = A5 segment of anterior cerebral artery
ACA = Anterior cerebral artery
AChA = Anterior choroidal artery
ACoA = Anterior communicating artery
ACoAA = Anterior communicating artery aneurysm
AdistA = Aneurysm distal to A3 segment of anterior cerebral artery
AIFA = Anterior internal frontal artery
AVM = Arteriovenous malformation
CI = Confidence interval
CMA = Callosomarginal artery
CRSR = Cumulative relative survival ratio
CSF = Cerebrospinal fluid
CT = Computed tomography
CTA = Computed tomographic angiography
DACA = Distal anterior cerebral artery
DSA = Digital subtraction angiography
ENT = Ear Nose & Throat
FPA = Frontopolar artery
GCC = Genu of corpus callosum
GCS = Glasgow coma scale
GDC = Guglielmi detachable coil
GOS = Glasgow outcome score
H&H = Hunt & Hess grade
IA = Intracranial aneurysm
ICA = Internal carotid artery
ICG = Indocyanine green
ICH = Intracerebral hematoma
ISAT = International Subarachnoid Aneurysm Trial
ISUIA = International Study of Unruptured Intracranial Aneurysms
IVH = Intraventricular hemorrhage
LSO = Lateral supraorbital approach
MCA = Middle cerebral artery
MIFA = Middle internal frontal artery
MLA = Medial lenticulostriate arteries
MRA = Magnetic resonance angiography
MRI = Magnetic resonance imaging
OFA = Orbitofrontal artery
OR = Odds ratio
PerA = Pericallosal artery
PCA = Posterior cerebral artery
PCoA = Posterior communicating artery
PICA = Posterior inferior cerebellar artery
PIFA = Posterior internal frontal artery
RAH = Recurrent artery of Heubner
RSR = Relative survival ratio
SAH = Subarachnoid hemorrhage
SD = Standard deviation
SMA = Supplementary motor area
SMR = Standardized mortality ratio
STA = Superficial temporal artery

List of original publications

This thesis is based on the following publications, referred to in the text by their Roman numerals:

I. Lehecka M, Porras M, Dashti R, Niemelä M, Hernesniemi J. Anatomic features of distal anterior cerebral artery aneurysms: a detailed angiographic analysis of 101 patients. *Neurosurgery* 2008, 63(2): 219–229.

II. Lehecka M, Lehto H, Niemelä M, Juvela S, Dashti R, Koivisto T, Ronkainen A, Rinne J, Jääskeläinen JE, Hernesniemi J. Distal anterior cerebral artery aneurysms: treatment and outcome analysis of 501 patients. *Neurosurgery* 2008, 62(3): 590–601 .

III. Lehecka M, Niemelä M, Seppänen J, Lehto H, Koivisto T, Ronkainen A, Rinne J, Sankila R, Jääskeläinen JE, Hernesniemi J. No long-term excess mortality in 280 patients with ruptured distal anterior cerebral artery aneurysms. *Neurosurgery* 2007; 60(2): 235–241.

IV. Lehecka M, Dashti R, Hernesniemi J, Niemelä M, Koivisto T, Ronkainen A, Rinne J, Jääskeläinen JE. Microneurosurgical management of aneurysms at A2 segment of anterior cerebral artery (proximal pericallosal artery) and its frontobasal branches. *Surg Neurol* 2008, 70(3): 232–246.

V. Lehecka M, Dashti R, Hernesniemi J, Niemelä M, Koivisto T, Ronkainen A, Rinne J, Jääskeläinen JE. Microneurosurgical management of aneurysms at A3 segment of anterior cerebral artery. *Surg Neurol* 2008, 70(2): 135–152.

VI. Lehecka M, Dashti R, Hernesniemi J, Niemelä M, Koivisto T, Ronkainen A, Rinne J, Jääskeläinen JE. Microneurosurgical management of aneurysms at A4 and A5 segments and distal cortical branches of anterior cerebral artery. *Surg Neurol* 2008, 70(4): 352–367.

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1. Introduction

Intracranial aneurysms (IAs) are acquired dilatations of intracranial arteries. They are typically located at the arterial branching points near the skull base. When an IA ruptures, it causes subarachnoid hemorrhage (SAH). Typical symptoms include sudden onset of severe headache, nausea, vomiting and often loss of consciousness. Risk factors for SAH include smoking, excessive alcohol consumption, hypertension and familial history [76,155,156]. SAH is a devastating event associated with cumulative mortality up to 50% at six months [84,131,381]. SAH represents only about 5–10% of strokes, but because the disease strikes at a fairly young age (≈ 50 yrs) and is often fatal, the loss of productive life years is similar to that for cerebral infarction and intracerebral hemorrhage [153]. The most important goal in the treatment of SAH patients is to prevent rebleeding from the ruptured aneurysm. At present, this is achieved by occluding the aneurysm either with microneurosurgical or endovascular methods.

Distribution of IAs along the different intracranial arteries is unequal so that certain arteries and their segments present more often with aneurysms than others, possibly due to flow related reasons. One of the infrequent aneurysm locations is the distal portion of the anterior cerebral artery (ACA), also called the pericallosal artery (PerA). Only about 6% of all IAs are found on this artery or on one of its cortical branches [52,122,142,205,248,279,312,368,383,438,445,449]. These aneurysms, located distally to the anterior communicating artery (ACoA) on the A2–A5 segments of the ACA and embedded between the cerebral hemispheres, are called distal anterior cerebral artery (DACA) aneurysms [122,198]. They have special features such as small size in concordance with the relatively small caliber of the DACA itself, and a broad base with originating branches, which have to be taken into account in their treatment, making especially endovascular therapy relatively difficult [52,122,205,248,279,312,368,383,438,443,449]. In addition, they are associated with vascular anomalies of the ACA, such as azygos, bihemispheric and triplicated pericallosal arteries, arteriovenous malformations (AVMs), and multiple aneurysms [122,133,383,438].

Microneurosurgery has been the treatment of choice for DACA aneurysms for several decades, whereas endovascular treatment has been used less frequently for the reasons mentioned above and only over the past fifteen years [184,265,300]. Although clipping has been the gold standard, the microsurgical series on DACA aneurysms published so far are relatively small [32,52,122,142,231,248,264,279,312,368,383,438,445]. The rarity of DACA aneurysms combined with the fact that they require a different microsurgical approach than other anterior circulation aneurysms [122,142,443] reduce opportunities to gain experience in the management of these aneurysms.

This study presents the combined experience of two Finnish neurosurgical centers (Helsinki and Kuopio University Hospitals) with population responsibility (of close to 3 million people), in a consecutive, retrospective series of 517 patients with DACA aneurysms treated between 1936 and 2007. This series of DACA aneurysms is by far the largest published to date. The data are based on an ethnically homogenous population with good medical records and complete follow-up of all patients. The aim is to provide new information on the anatomic features, treatment, microneurosurgical techniques, outcome, and long-term follow-up of DACA aneurysms, also in comparison to the matched general population.

2. Review of literature

2.1. Intracranial aneurysms

2.1.1. Prevalence of intracranial aneurysms

Intracranial aneurysms (IAs) are found in about 2% of the general adult population, and are considered to be acquired lesions [328]. In Finland (population 5.3 million) the standardized prevalence is estimated to be 2.2–3%, implying that 100 000 Finns would carry unruptured IAs [336]. Most of the aneurysms are saccular (97%) and arise at sites of arterial branching [49]. Women are more likely to harbor an IA than men (relative risk = 1.3), and this proportion increases with age [328]. Also, in families with two or more members affected with IAs, the risk of having an IA is 2–4 times higher than what is expected in a general western population [335]. Multiple aneurysms are usually found in 28–35% of patients with IAs [49,50,70,140,331].

2.1.2. Pathobiology of intracranial aneurysms

2.1.2.1. Morphology and formation of intracranial aneurysms

IAs are usually divided into two groups based on their morphological features: (a) saccular aneurysms, which are pouch-like protrusions of the vessel wall usually found at the bifurcations of the intracranial arteries and comprise 97% of all IAs; and (b) fusiform aneurysms, which are dilatations of the whole arterial segment with neither a distinguishable base nor a separate pouch, comprising about 3% of all IAs [47,48]. A small number of fusiform aneurysms are dissecting in origin. Although the exact pathobiological mechanism of IA formation is still unknown, IAs are believed to be acquired lesions. Some are caused by direct vascular trauma (traumatic aneurysms) [19,261], or bacterial infection (mycotic aneurysms) [35,86,201], but in the vast majority of cases, a combination of multiple factors are probably involved, including hemodynamic stress acting on the vessel wall [85,129], inflammation processes [89,411], arterial wall remodeling and degeneration [88,203], and a multitude of extrinsic risk factors such as smoking, hypertension, alcohol consumption and genetic predisposition [76,161,421], which cause the IA formation and growth.

2.1.2.2. Genetics of intracranial aneurysms

The concept of genetic factors being involved in the development of aneurysms has lead to many studies on the genetic determinants for IA. So far, different genome-wide linkage studies have identified several loci [344], but only four (1p34.3–p36.13, 7q11, 19q13.3 and Xp22) have been replicated in different populations [75,246,259,283,284,345,420,439]. Knowledge on the genetic determinants may provide insight into the development of aneurysms, and thereby give clues on how to stop aneurysm formation. It may also provide diagnostic tools for identifying individuals at increased risk for aneurysm formation who can be screened by imaging studies. In the near future, whole-genome mutation analysis will probably give more data.

2.1.2.3. Histology of intracranial aneurysms

Normal intracranial arteries are composed of three histological layers: loose connective tissue layer (adventitia); muscular layer of smooth muscle cells (media); and inner layer of endothelial cells and smooth muscle cells (intima) [341]. There is also a very thin layer of elastic fibers, the internal elastic lamina, at the border between the media and intima. IAs usually have a disorganized wall structure and lack elastic laminae [175,196]. Four dominant histo-

logical wall types of IAs have been recognized: (A) endothelialized wall with linearly organized smooth muscle cells; (B) thickened wall with disorganized smooth muscle cells; (C) hypocellular wall with fresh or organizing thrombosis; and (D) extremely thin thrombosis-lined hypocellular wall [89]. Many aneurysm walls are heterogeneous, constituted by a combination of the different wall types, but the C and D types are predominant in ruptured aneurysms [89]. The histological differences between ruptured and unruptured IAs suggest that the aneurysm wall is a dynamic structure undergoing constant remodeling [88]. Complement activation seems to associate with degeneration and rupture of IAs [411]. Also protein kinases (c-Jun N-terminal kinase and p38 kinase) are involved in the growth and rupture of IAs [203]. A better understanding of the molecular mechanisms behind IA formation and rupture may provide possibilities of targeted pharmacological therapy for IAs in the future.

2.1.3. Subarachnoid hemorrhage

Subarachnoid hemorrhage (SAH) due to rupture of an IA is a devastating event associated with high rates of morbidity and 50% mortality [131]. SAH accounts for 5–10% of all strokes, but as the disease strikes at a fairly young age (mean age 50 years) the loss of productive life years can be significant [153,190]. Besides IAs (80–85%), SAH can also be caused by AVMs (5%), or an unknown etiology (15%) [172,334,353]. In the latter case, the prognosis is very good.

2.1.3.1. Incidence of SAH

The incidence of SAH varies in different populations. In most populations the incidence is 6–10 cases per 100 000 person-years [7,218]. For unknown reasons, probably genetic, in Finland, Japan and Northern Sweden the incidence is much higher with 16–20 cases per 100 000 person-years [84,138,277,369,381]. This means that in Finland about 1000 patients suffer from SAH every year. With almost 50% mortality, more people in Finland die annually because of SAH than due to traffic accidents. In 2006, there were 365 deaths due to SAH compared to 307 deaths from traffic accidents [379].

2.1.3.2. Natural history of ruptured intracranial aneurysms

About 15% of the SAH patients die before reaching medical attention [132,290,301]. In the historical, unselected series by Pakarinen the cumulative mortality was 32% during the first day, 46% during the first week, 56% during the first month and 60% during 6 months [290]. The initial hemorrhage causes the greatest mortality [84], being also the reason why even with the advent of new treatments the case-fatality rate of SAH has been declining very slowly [131,369,381]. If the aneurysm is left untreated, about one third of the patients who recover from the initial hemorrhage will die of rebleeding during the first 6 months [124,290,298]. Delayed cerebral vasospasm is the second major cause of death in patients surviving the initial ictus [106,170]. Even with modern treatment, case-fatality rates are still close to 50% at one month after SAH [131,301,369,381]

2.1.4. Treatment of ruptured intracranial aneurysms

Treatment of ruptured IAs focuses on three major issues: (a) to prevent rebleeding; (b) to prevent delayed vasospasm; and (c) to take care of all the additional problems caused by the initial impact of SAH.

2.1.4.1. Rebleeding

The peak incidence of rebleeding occurs during the first 24 hours when the risk is 4–7% [141,158,171,290]. After this the risk remains at 1–2% per day for the following two weeks,

and for the first month the cumulative risk is 30–35%. The problem with rebleeding is that about 60% of the patients who have a rebleeding die [141,158,171,290]. The best method to prevent rebleeding is intervention with either microneurosurgical or endovascular approach [237,250]. Early surgery combined with nimodipine (calcium antagonist) treatment has been shown to reduce both the rebleeding rate and the risk for vasospasm [278]. By preventing early rebleeds, early surgery both decreases the mortality rate and improves the quality of life of the survivors [84].

2.1.4.2. Cerebral vasospasm

Cerebral vasospasm is defined as delayed narrowing of intracranial arteries often associated with diminished perfusion in the territory of the affected artery ultimately leading to hypoxia [237]. Angiographic vasospasm is detected in 50–75% of the patients with a typical onset of three to five days after SAH [139,170]. Without treatment about half of these patients develop clinical symptoms of ischemic neurological deficits and some even die [125]. Combined mortality and morbidity associated with cerebral vasospasm is about 15% of all SAH patients [106,222]. So far, no single treatment to prevent vasospasm really effectively has been identified.

2.1.4.3. Other complications of SAH

Additional complications related to acute SAH include hydrocephalus, expansive intracerebral hematomas (ICHs), hyponatremia, seizures, and less frequently also cardiac arrhythmia, cardiac dysfunction, myocardial injury, pulmonary edema, acute lung injury, renal dysfunction, and hepatic dysfunction [48,49,111, 112,123,329,377,388,393,413]. This shows how SAH not only affects the brain but also has an impact on almost the whole body.

2.1.5. Outcomes for ruptured IAs

2.1.5.1. Outcome assessment

Results of management outcomes in patients with SAH from a ruptured IA have not been reported in a standardized manner. In population based studies, outcome is often measured by the cumulative case-fatality rate at one to six months after SAH [131,290,301,369,381]. The case-fatality rate allows observation of trends over long periods of time but it does not take into account the functional state of the patient. Most studies evaluating treatment of SAH use either the Glasgow outcome score (GOS) [152], or the Rankin scale [322], both of which divide patients into categories based on their functional capacity.

2.1.5.2. Treatment outcome

Although the case-fatality rates of SAH have been slightly declining over the last three decades [131], they are still as high as 35–50% [84,301,381]. The outcome depends strongly on the admission policy of the hospital and especially on the proportion of poor-grade patients. Many large surgical series from referral centers are strongly biased towards patients in better preoperative condition [430]. In centers with active admission policy and little selection bias so that even poor-grade patients are treated, 60–80% of patients had a favorable outcome (GOS≥4) [123,193,350,356]. It is even more difficult to compare outcome of surgical treatment in between different patient series as there are many factors causing selection bias. These include clinical condition before treatment, aneurysm location, timing of treatment, methods for outcome evaluation, length of follow-up, and prospective vs. retrospective nature of the data.

2.1.5.3. Predictors for outcome after SAH

Factors which are generally recognized to predict outcome after SAH are: neurological grade on admission, age, amount of blood on

the preoperative CT scan, intracerebral hematoma (ICH), intraventricular hemorrhage (IVH), and aneurysm location [339]. The neurological grade on admission has the strongest effect on outcome [260,287,329,342]. In patients with initial clinical grade IV or V, a favorable result was seen in only 30–50% of the cases irrespective of the treatment method [28,173,204,249,426], whereas good preoperative clinical grade (Grade I or II) predicted a favorable result in 80–90% of the patients [123,173,287,350]. The second most important factor is the age [339]. Younger patients seem to be more likely to tolerate systemic stress caused by acute SAH and, therefore, recover better than the elderly [207,287,329,342]. Thick blood clots in basal cisterns (Fisher grade≥3), a risk factor for development of delayed vasospasm [80], also predict a less favorable outcome [110]. Neurological grade, age and blood on CT scan seem to be more important than other factors in predicting the outcome after SAH [339].

2.1.6. Long-term follow-up after SAH

2.1.6.1. De novo aneurysms and rebleeding

The risk of rebleeding from a treated aneurysm is of major concern for a patient after microsurgical or endovascular treatment. Multiple aneurysms, usually present already at the first SAH or rarely developing later (*de novo*) [332], are detected in about one third of SAH patients [331]. They are considered to be a predisposing factor for recurrent SAH together with smoking and hypertension [428]. The cumulative rupture rate increases with follow-up and the relative risk compared to the general population is higher [160,419].

De novo aneurysms developed with the annual rate of 0.84% in a previous Finnish study with a median follow-up time of 19 years [161]. In a Japanese study, the annual rate of *de novo* aneurysm formation was 0.89%, being much higher than the 0.26% rate for re-growth of completely clipped aneurysm [408]. The International Study of Unruptured Intracranial Aneurysms (ISUIA) suggested a 5-year cumulative rupture rate of 1.5% for unruptured anterior circulation aneurysms in patients with previous SAH [431]. A recent study from The Netherlands states the incidence of recurrent SAH after clipping of ruptured aneurysms in a 10-year follow-up as 3.2% with 77% due to de novo aneurysms [427]. Unfortunately, there are no population based studies on SAH with median follow-up times of over 15-20 years. The present belief is that patients with multiple aneurysms and a history of SAH are at increased risk of developing new aneurysms in the long run [157,159], but these aneurysms are likely to have the same rupture risk as other unruptured aneurysms.

2.1.6.2. Long-term mortality

Relatively little is known about the long-term survival after aneurysmal SAH. Most studies report long-term outcome as early as 6 or 12 months after SAH [7,105,131,338]. There are only two population based SAH studies with a median follow-up of over 5 years. Ronkainen et al. showed that Finnish SAH patients with good recovery at 12 months and successful treatment of their ruptured aneurysm had mortality rate twice as high as the general population during a median follow-up of 7.5 years [337]. Olaffson's series of 44 Icelandic patients who survived over 6 months after SAH showed that the patients who had severe disability at 6 months experienced excess mortality during the first 10 years of follow-up [281]. Both of these studies included all SAH patients irrespective of the location of the aneurysm.

2.1.7. Management of unruptured IAs

In the management of patients with unruptured IAs the risk of treatment has to be weighed against the risk of rupture and subsequent complications. Annual rupture rate for unruptured aneurysms has been estimated to

be about 1% [160,161,328,448]. Risk factors for aneurysm rupture include the female gender, smoking, older age, high blood pressure, aneurysm size, aneurysm location, and country of origin [76,155,159,160,218,317,328]. Of these, smoking seems to have the highest attributable risk of almost 50% and even if smoking is stopped, the risk of SAH remains higher than in nonsmokers [76,189]. The largest study on unruptured aneurysms with 4060 patients and mean follow-up of four years, the ISUIA study, identified in the multivariate analysis of their prospective cohort only the aneurysm size and location as predictors for rupture, although there was some selection bias of aneurysm location between the conservatively and actively treated groups [431]. In a meta-analysis of surgical series from 1970 to 1996, the mortality and morbidity rates related to treatment of unruptured IAs were 2.6% and 11%, respectively [317], but the giant and posterior circulation aneurysms were overrepresented in this analysis so that for most aneurysms the risk is probably lower [154]. The ISUIA study reported 1.5–2.3% mortality and 10–12% morbidity in a prospective follow-up [431]. It seems that an appropriate risk/benefit analysis requires thorough knowledge of the treatment results of the particular center or the physician giving the treatment. Unlike in ruptured aneurysms, where the initial impact of SAH strongly determines the management outcome, in unruptured aneurysms it is the experience, knowledge and skills of the treating physician and his team that have the main impact on the outcome [194]. In Finland, with higher rupture risk, even small, unruptured aneurysms are treated actively, microneurosurgery being often preferred over endovascular treatment due to the high proportion of middle cerebral artery (MCA) aneurysms (40%) [49], and the better long-term results associated with clipping [251].

2.2. History of intracranial aneurysm treatment

2.2.1 Before microneurosurgery

2.2.1.1. Intracranial aneurysms in historical context

Found in the Ebers Papyrus and attributed to Imhotep (2725 BC), the first record of an arterial aneurysm described the treatment of a bulging aneurysm with a fire-glazed instrument by an Egyptian physician [219]. In 117 BC, Flaenius Rufus, a physician from Ephesus and trained in Alexandria, made a notion that arterial dilatation could be caused by trauma [51], but it was the Greek physician Galen of Pergamum who first properly defined and described the entity of an arterial aneurysm in general in 200 AD [225]. During the next 1500 years, Islamic physicians expanded their knowledge on aneurysms, their origins and sites, whereas in the western cultures studies on human anatomy were largely stagnant for both religious and cultural reasons [168,169]. The modern definition of aneurysm as a dilatation of a weakened artery was made by Lancisis in 1728 [429]. Intracranial aneurysms were definitely described for the first time in the autopsy reports by Morgagni (1761, Padua), Biumi (1765, Milan), and Blane (1800, London) [22,27,256]. At that time there were no reports on their treatment as the IAs were usually found only at post mortem examinations. It was not until Heinrich Quincke introduced the lumbar puncture in 1891 [314] that the diagnosis of SAH became truly possible in living patients, a development which in turn led to substantial discussions about the possibilities of treating patients with aneurysmal SAH.

2.2.1.2. Hunterian ligation

In 1805, Cooper performed carotid ligation for an extracranial carotid artery aneurysm with a fatal result [39]. Undeterred, he performed the same procedure three years later, this time suc-

cessfully [38,40]. Arterial ligation in general was popularized in the 18th century by John Hunter who demonstrated a safe and reproducible means of proximal femoral artery ligation for popliteal aneurysms as an alternative to leg amputation [136]. Named in his honor, Hunterian ligation of the internal carotid artery (ICA) was adopted by many surgeons as a method for treating intracranial vascular pathologies. In 1809, Benjamin Travers was the first to report a successful treatment of an intracranial lesion (carotid cavernous fistula) by this method [403], but it was much later before the Hunterian ligation was used to treat an actual IA.

2.2.1.3. Carotid occlusion

In 1885, in London, Sir Victor Horsley operated on a 48-year old woman thought to suffer from a tumor in the middle cranial fossa. Intraoperative finding was a pulsating mass, most likely an aneurysm, which forced Horsley to change his surgical strategy. Instead of removing the lesion, he ligated the right common carotid artery. The patient was reported to be doing well five years later [180]. Many surgeons after Horsley ligated the ICA on encountering an IA during an intracranial operation. However, these ligations were quite frequently followed by cerebral infarctions, which led to the need of differentiation of patients who would tolerate occlusion. Matas developed a preoperative compression test for this purpose in 1911 [236], but it was not until 1924 that the first planned ICA ligation for IA, diagnosed preoperatively, was carried out by Trotter on a patient with traumatic aneurysm causing severe epistaxis [354]. A variety of more sophisticated techniques were developed over the following years to allow gradual occlusion of the carotid artery while building up the collateral circulation including Matas's band from aluminum strips, double fascia band, and Neff's clamp [235,263,297,307]. Later on came the Dott, Crutchfield, Selverstone, and Kindt clamps, some of which remained in use until the late 1970s when they were outdated first by microneurosurgery and later by endovascular surgery [42,63,95,358]. Even with gradual occlusion of the carotid artery by these different clamps, the mortality rates were around 20% and the stroke rate was as high as 30% [268,306,354].

2.2.1.4. Cerebral angiography

The introduction of cerebral angiography by António Egas Moniz in 1927 not only revolutionized the diagnostics of cerebral aneurysms but also played a key role in starting the development of IA treatment [253]. Before that, plain x-rays, pneumoencephalography, and myelography were the basic imaging methods of the central nervous system. In this way only some calcified aneurysms could be seen and even those were initially often mistaken for tumors such as calcified meningeomas. By 1931, Moniz was able to perform a complete carotid angiogram including arterial and venous phases, and two years later, he published an article on IA diagnostics by means of angiography [252]. In the same year, Dott was the first to operate on an aneurysm previously diagnosed by angiography [62]. Initially, one of the problems associated with angiography was the radioactivity of Thorotrast®, the contrast medium used at that time, which remained in the liver and in fact proved to be carcinogenic [303]. This contrast agent was exchanged for a 35% Diodrast® solution, the intravenous pyelogram contrast medium, which, turning out to be much safer, became widely accepted [305,451], though still far from being comparable to the modern contrast media [58]. Although Moniz had opacified even the posterior circulation by an open retrograde subclavian injection, it was Krayenbühl in 1941 who first demonstrated an aneurysm on the vertebro-basilar system using the same method [351]. Angiography's usefulness as a diagnostic tool increased even further with the percutaneous carotid puncture technique described by Lohman and Myerson in 1936 and Shimidzu in 1937 [221,402], and later with

Seldinger's technique of catheter angiography through the percutaneous transfemoral route published in 1953 [357].

2.2.1.5. Wrapping and trapping

Norman McComish Dott of Edinburgh (a pupil of Cushing's) was the first to be credited with direct attack on a ruptured aneurysm in 1931. Without angiographic assistance, he performed a frontal craniotomy on a 53-year old patient, who was the financial director of Dott's hospital with three previous bleeds and a III nerve palsy. Intraoperatively, a 3-mm aneurysm in the region of ICA bifurcation was wrapped with muscle harvested from the patient's thigh, and the patient made a good recovery [62]. Additional reports by Tönnis, Dandy, and Jefferson added to the literature on wrapping [44,151,398]. Herbert Olivecrona, founder of Scandinavian neurosurgery, was the first to effectively treat a posterior circulation aneurysm in Stockholm in 1932. During operation on what he initially thought to be a posterior fossa tumor, he found a large, thrombosed posterior inferior cerebellar artery (PICA) aneurysm, which he trapped and excised [270]. The patient was reported to be doing well 17 years later [220]. In 1936, Dandy invented a new technique to treat an ICA aneurysm in or near the cavernous sinus by ligating ICA both intracranially and extracranially, thus trapping the aneurysm [45].

2.2.1.6. Clipping

A major revolution in the treatment of IAs came with the invention of metallic clips [302]. In 1911, in his quest to develop tools for tumor resections, Harvey Cushing produced what was to become known as "the silver clip" or "Cushing clip" [43]. Cushing used this clip in tumor surgeries for "placement on inaccessible vessels, which, though within reach of a clamp, are either too delicate or in a position too awkward for safe ligation" [43]. The original silver clip, made out of round silver wire, was first modified in 1927 by McKenzie into a V-shaped clip using flat wire [243], and later in 1949 by Duane into a U-shaped clip [66]. Cushing never used his invention for intracranial aneurysm surgery, instead, it was his competitor Walter Dandy who clipped the first aneurysm on March 23rd 1937 [46]. He exposed a saccular posterior communicating artery (PCoA) aneurysm causing oculomotor palsy, and clipped the aneurysm at the neck with a Cushing-McKenzie type silver clip. The oculomotor palsy subsided six weeks later [46]. This new clipping method allowed neurosurgeons to exclude an aneurysm selectively from the intracranial circulation, a concept that marked the beginning of the modern era of aneurysm surgery.

2.2.1.7. Aneurysm clip development

The clip used by Dandy in 1937 evolved significantly over the next decades. First there was the development of an adjustable clip which could be re-opened and repositioned, a winged clip with a special applicator modified by Olivecrona [271]. The mechanism of crossing the legs of a spring forceps was invented already in 1840 by the French medical instrument maker Joseph Charrière [242], and the idea became the basis for even the modern-day clips. Schwartz introduced a miniature spring forceps clip to allow re-opening of the clip to prevent shearing and tearing of the aneurysm base [238]. As Schwartz's clip was robust and the applicator was awkward to enable effective use intracranially this led Mayfield and Kees to modify the cross-legged clip in 1952 into a tool designed specifically for aneurysm surgery [238]. The Mayfield clips were produced with different lengths and angulations, and gained wide popularity among neurosurgeons practicing aneurysm surgery [238]. Over the following decades, substantial modifications were made as various neurosurgeons suggested improvements [224]. McFadden suggested round instead of flat blades [238], while Sundt and Nofzinger developed a Teflon-lined, ves-

sel encircling clip-graft in 1967 [389], and in 1969 Kees made the first fenestrated clips for Drake's needs [64]. Scoville produced a miniature torsion-bar aneurysm clip in 1966 [355], and Heifetz designed a clip with an internal wire spring in 1968 [115]. Interestingly, the original idea behind the Heifetz clip came from a Finnish neurosurgeon, Stig Nyström, who invented a silver aneurysm clip with an internal spring in 1959 (S Nyström, personal communication) [275]. Nyström and a few others used these clips which, however, never gained widespread popularity since obtaining a patent for this kind of product was very difficult at that time in Finland (S Nyström, personal communication). The Heifetz clip was similar in design to the Nyström clip, though somewhat more delicate, but the biggest difference was that it was made from steel. The clip design with the longest life cycle so far originated from the collaboration between McFaden and Kees in 1970 [241]. This design implemented a mechanism to prevent scissoring, and an additional spring loop to increase the closing force while allowing the whole clip to be made from the same material [240]. Later, other neurosurgeons such as Yaşargil, Sugita, Drake, Perneczky, and Spetzler have been intensively involved with modifying the aneurysm clips to better suit the specific needs of microneurosurgery [213,214,296,302, 387,447]. It is important to note that especially in the 1950s and 1960s, before the Mayfield clips came to wide use, many aneurysms were tied at the neck with linen or silk thread [23].

2.2.2. Microneurosurgery

2.2.2.1. Operating microscope

In the latter half of the 19th century, microscopes were already used in industry and scientific research, but in clinical surgery their use was preceded by loupe magnification. True compound magnification was used for the first time in surgery by the German physician Saemisch, who wore loupes in 1876 [363]. In 1921, the Swedish otolaryngologist Carl Nylen, inspired by a paper of Maier and Lion on observations of endolymph movements in the ears of live pigeons using a dissecting microscope, conceived, built and used the world's first surgical monocular microscope [59,274]. This invention was followed the next year by his chief Gunnar Holmgren, who attached an external light source to an existing Zeiss dissecting microscope, thus introducing the first binocular surgical microscope [59]. The original surgical microscopes were rather robust, had a limited field of vision, lacked stable and freely movable support, and had an insufficient coaxial light source [325]. In the early 1950s, several technical advancements encouraged microscopes to be used more frequently. Hans Littman of Zeiss Company developed the optical design for changing magnification without changing the focal length and he designed the first series-produced operating microscope, Zeiss OpMi 1 (Zeiss Operating Microscope Number One) in 1953 [128,228]. Later in 1960, it was again Littman who designed the first two-person series-produced operating microscope, the diploscope, for the microsurgical laboratory in Burlington, Vermont [200].

2.2.2.2. Development of microneurosurgery

On August 1st, 1957, Theodore Kurze, at the University of Southern California in Los Angeles, was the first neurosurgeon to use a microscope in the operating room [61,200]. A year later, Raymond Madiford Peardon Donaghy established the world's first microsurgery research and training laboratory in Burlington, Vermont [61,200,239,425]. He was interested in treating cortical strokes by removing clots from inside the thrombosed artery and repairing it afterwards. He collaborated with a vascular surgeon, Julius Jacobson, first using the Zeiss OpMi 1 borrowed from the ENT services [29,61]. Later, with the help of the diploscope designed by Littman and special sets of instruments developed for microsurgery, Jacobson and Suarez

successfully anastomosed carotid arteries in dogs and rabbits, and published their findings on the power of microscope in small-vessel anastomoses in 1960 [144,145,385]. The same year, Donaghy used the operating microscope to perform the first embolectomy and endarterectomy on the middle cerebral artery [145]. In 1962, a cardiac surgeon in Zürich, Åke Senning, asked neurosurgeon Hugo Krayenbühl to remove an embolus from the MCA in a young patient with hemiplegia after cardiac surgery. At that time Krayenbühl did not think this possible, but the idea of surgery on small intracranial vessels remained and in 1965 he dispatched his pupil, M. Gazi Yaşargil, to the United States to learn the new art of microsurgery [60]. Yaşargil originally approached Jacobsen, who referred him to Donaghy's laboratory in Vermont, where he spent the next year mastering microsurgical techniques under the guidance of Miss Esther Roberts by means of performing anastomoses of the superficial temporal artery (STA) to the middle cerebral artery (STA-MCA bypass) in dogs [60,61]. Upon returning back to Zürich, Yaşargil performed the first STA-MCA bypass on a human patient on October 30th, 1967 [60]. Less than 24 hours later, Donaghy performed the same operation in Burlington, and both of these surgeries were successful [61]. Yaşargil's return to Zürich and the first microsurgical operation on February 1st 1967 marked the beginning of a new era in microneurosurgery. Yaşargil's devotion to development of operative approaches, techniques and instrumentation has been appraised by many of his colleagues [82,394]. In 1979, Donaghy wrote: "Little was it realized at this time (in 1965), even by Hugo Krayenbühl, that this young Turk was destined to do more for the development of microneurosurgery in the human nervous system than any other man" [61].

2.2.2.3. Other technical developments

Microneurosurgery was very much dependent on technical and anesthesiological innovations. On the microscope front, Yaşargil's collaboration with the Contraves Company resulted in designing a counterbalanced stand for microscope, originally suggested by Malis, with a system of electromagnetic brakes permitting full mobility and perfect stability [230,447]. The major advantage of microscopes, a clear, bright, 3D magnified vision, required a bloodless operating field. This could be obtained with the bipolar coagulator, first described by Greenwood in 1940, and subsequently improved by Malis [100,101,228–230,239]. Compared to unipolar coagulation, in which the current spreads over a larger area, bipolar coagulation allows to limit the coagulation to precisely targeted structures. In addition, the bipolar forceps could serve as a general dissection instrument [230,447]. Microsurgical instrumentation has evolved gradually from the early days of microsurgery to reach the highly sophisticated level of the present time. But even the best technical advances would not have sufficed without the developments in balanced neuroanesthesia with constant monitoring of different physiological parameters [321]. The introduction of controlled hyperventilation and effective osmotic agents, first urea in 1954 by Javid [148–150], and later mannitol in 1961 by Wise and Chater [364,436,437], provided additional space for intracranial procedures and diminished the grave dangers of opening the dura in the presence of a tight brain. These achievements also paved the road for the concept of early surgery in ruptured aneurysms.

2.2.2.4. Microneurosurgery applied to intracranial aneurysms

Microsurgery started expanding into aneurysm surgery in the 1960s. Kurze was the first to use the microscope systematically for all his aneurysm cases starting in 1958, but he never published or presented his series [200]. Adams and Witt started using an ENT microscope for aneurysms in 1963 and presented their experience at the meeting of the Neurosurgical

Society of America in 1964 [3]. The first published series on aneurysm surgery using a microscope came from Pool and Colton in 1966, who published their experience in 13 patients [304]. The next year Rand and Janetta reported a basilar bifurcation and a PICA aneurysm, both ligated with silk thread under the microscope [320]. They emphasized the power of microscope in distinguishing the small perforators in basilar bifurcation aneurysms and compared their experience with Drake's, who at that time had a 50% mortality in his series of eight basilar bifurcation aneurysms operated without the microscope but with loupes [65]. Microneurosurgery was spreading fast during this period as an increasing number of neurosurgeons realized the advantages of microsurgery on their results. Publications by Lougheed (1969), Cophignon (1973), Hollin (1973), and Guidetti (1973) totaled 236 anterior circulation aneurysms operated on under the microscope [41,104,130,223]. The real groundbreaking series was that by Krayenbühl and Yaşargil in 1972, describing Yaşargil's results over a four-year period from 1967 to 1971, in which total mortality was only 4% in 231 patients with microsurgically operated anterior circulation aneurysms [199]. With further experience and development of instrumentation mortality in Yaşargil's series dropped to 2% in the time period from 1970 to 1974, setting a new standard for aneurysm surgery (late surgery) [446]. Meanwhile Drake, already using a microscope (since 1970), pioneered surgery for posterior circulation aneurysms [64].

2.2.3. Endovascular surgery

2.2.3.1. Balloon occlusion

The first attempts to cure brain aneurysms from the endovascular side using injection of either hog or horse hair into the aneurysm sac during open surgery were reported by Gallagher in 1964 [94]. His idea was that the shingles on the end of the hair, placed inside the aneurysm, would create a mechanical nidus for clotting, yet complete thrombosis of the aneurysm occurred in only nine of the 15 patients [94]. In 1971, Serbinenko, a Russian neurosurgeon from the Burdenko Institute in Moscow, reported the use of inflatable balloons for temporary occlusion of intracranial vessels and carotid cavernous fistulae [361]. By 1974, he reported the use of selective catheterization to deliver and deploy detachable balloons filled with a hardening agent (liquid silicone) for the treatment of various intracranial vascular lesions, including aneurysms, in more than 300 patients [360]. Although initially a promising method, significant complications and recanalization of aneurysms were later reported even when using other material to fill the balloon [57,126,127,254,333]. A big step in endovascular therapy came with the introduction of microcatheters and microguidewires by Target Therapeutics (Fremont, CA, USA) in 1986, which allowed safer and more effective exploration of intracranial vessels [182].

2.2.3.2. Coiling

The most important technical development in endovascular surgery for the treatment of IAs was the invention of Guglielmi detachable coils (GDC) in 1990 [102,103]. The initial coils for endovascular use were available as free coils, i.e. they had to be pushed through the microcatheter with a special wire referred to as the coil pusher, and once they left the tip of the catheter they could not be pulled back [326]. Guglielmi, together with Sepetka, developed the first generation of electrolytically detachable platinum coils allowing proper positioning inside the aneurysm before the release [103]. In 1991, Guglielmi published the first series of 15 patients treated with this new method [102]. The method spread fast and several large series on the use of GDCs in aneurysm treatment were published in the following years [36,424]. Owing to the development of new techniques, such as balloon remodeling technique intro-

duced by Moret in 1997 [255], and introduction of new coils and other embolic material, an increasing number of aneurysms could be treated by endovascular methods [309]. This also started a competition between microneurosurgery and endovascular surgery forcing supporters of either technique to seek faster, safer, less invasive, and more durable techniques of IA treatment for the benefit of the patients [121].

2.2.4. Aneurysm surgery in Finland

2.2.4.1. Aarno Snellman, founder of Finnish neurosurgery

The first neurosurgical operations in Finland were performed in the beginning of the 20th century by surgeons such as Schultén, Krogius, Faltin, Palmén, Kalima and Seiro, but it is Aarno Snellman who is considered the founder of neurosurgery in Finland [400]. The Finnish Red Cross Hospital, which was the only center for Finnish neurosurgery until 1967, was founded in 1932 by Marshall Mannerheim as a trauma hospital [401]. Already during the first years, the number of patients with different head injuries was so significant that an evident need for a trained neurosurgeon and specialized nurses was soon identified. In 1935, Professor of Surgery Simo A. Brofeldt sent his younger colleague, 42-year old Aarno Snellman, to visit Olivecrona in Stockholm [401]. Snellman spent there half a year, closely observing Olivecrona's work. Upon his return, he performed the first neurosurgical operation on September 18th, 1935 [401]. This event is generally considered as the true beginning of neurosurgery in Finland.

2.2.4.2. Angiography in Finland

The initially relatively poor surgical results were mainly due to insufficient preoperative diagnostics. Realizing the importance of preoperative imaging Snellman convinced his colleague from radiology, Yrjö Lassila, to visit Erik Lysholm in Stockholm [400]. The first cerebral angiographies were performed after Lassila's return to Helsinki in 1936 [375]. At that time, angiography was often performed only on one side as it required surgical exposure of the carotid artery at the neck and four to six staff members to perform the relatively lengthy procedure: one to hold the needle, one to inject the contrast agent, one to use the X-ray tube, one to change the films, one to hold the patient's head, and one to show light. The procedure was quite risky for the patient, and there was one death among the first 44 cases (2% mortality) [375]. There were also some quite unexpected complications such as the situation where the surgeon injecting the contrast agent got an electric shock from the X-ray tube, fell unconscious to the floor, and while falling, accidentally pulled the loop of the silk thread passed under the patient's carotid artery, thus causing total transection of this artery. Fortunately, the assistant was able to save the situation and, as Snellman stated in his report, "no one was left with any permanent consequences from this dramatic situation" [375]. Before 1948, the number of cerebral angiographies was only 15–20 per year [402], but with the introduction of percutaneous technique at the end of 1948, the number of angiographies started gradually to rise with more than 170 cerebral angiographies performed in 1949 [402].

2.2.4.3. World War II and the late 1940s

World War II had a significant effect on the development of neurosurgery in Finland. On the one hand, the war effort diminished the possibilities to treat the civilian population, on the other hand the high number of head injuries boosted the development of the neurosurgical treatment of head trauma [401]. During this period, several neurosurgeons from other Scandinavian countries worked as volunteers in Finland helping with the high casualty load. Among others there were Lars Leksell, Nils Lundberg and Olof Sjöqvist from Sweden, and Eduard Busch from Denmark [400]. After the

war, it became evident that neurosurgery was needed as a separate specialty. Aarno Snellman was appointed Professor of Neurosurgery at the Helsinki University in 1947, and in the same year, the medical students had their first, planned course in neurosurgery [374]. The next year, Teuvo Mäkelä, who worked in neurosurgery since 1940 in charge of head injury patients, was appointed First Assistant Professor of Neurosurgery [400]. An important administrative change came in 1946, when the Finnish government decided that the state would pay the expenses of neurosurgical treatment [401]. With this decision neurosurgical treatment became, at least in theory, available for the whole Finnish population. The limiting factors were hospital resources (there was initially only one ward available) and the relatively long distances within the country. This explains partly why, especially in the early years, e.g. aneurysm patients sought operative treatment several months after the initial rupture, and only those in good condition were selected. Neurosurgery remained centralized in Helsinki until 1967, when the department of neurosurgery in Turku was founded, to be later followed by neurosurgical departments in Kuopio (1977), Oulu (1977) and Tampere (1983) [406].

2.2.4.4. Initial steps in aneurysm surgery

Aneurysm surgery in Finland started relatively slowly. In 1939, from among the first 44 patients undergoing diagnostic angiography at the Neurosurgery Department in Helsinki, only nine were diagnosed with an IA [375]. It is difficult to establish the exact date of the first aneurysm surgery in Finland. In their paper on 52 MCA aneurysms from 1958, af Björkesten and Troupp mention a patient who was operated on in 1937, and who subsequently died from wound infection [25]. Unfortunately, they neither specified the exact date nor the surgical procedure used. During World War II, the main focus of Finnish neurosurgery was, as stated before, on traumatology. Later, the better avail-

Table 1. *The early publications from Helsinki on the treatment of intracranial aneurysms.*

Year	Author(s)	Journal	Publication
1957	af Björkesten and Troupp [26]	*J Neurosurg*	Prognosis of subarachnoid hemorrhage, a comparison between patients with verified aneurysms and patients with normal angiograms
1958	af Björkesten and Troupp [25]	*Acta Chir Scand*	Aneurysms of the middle cerebral artery, a report on 52 cases
1958	af Björkesten [23]	*J Neurosurg*	Arterial aneurysms of the internal carotid artery and its bifurcation, an analysis of 69 aneurysms
1959	Snellman, Mäkelä and Nyström [373]	*Neuro-Chirurgie*	Considerations on the aneurysms of the anterior communicating artery, a report on 52 cases [in French]
1960	Laitinen and Snellman [205]	*J Neurosurg*	Aneurysms of the pericallosal artery, a study of 14 cases
1960	af Björkesten and Troupp [24]	*Acta Chir Scand*	Multiple intracranial arterial aneurysms
1961	Laitinen and Troupp [206]	*Acta Neurol Scand*	Reliability of partial ligation in the aneurysm treatment of intracranial arterial aneurysm
1962	Heiskanen [117]	*Acta Neurol Scand*	Large intracranial aneurysms
1964	Troupp and Laitinen [407]	*Acta Neurol Scand*	Reliability of partial ligation in the aneurysm treatment of intracranial arterial aneurysm. II
1971	Troupp and af Björkesten [405]	*J Neurosurg*	Results of controlled trial of late surgical versus conservative treatment of intracranial arterial aneurysms

ability of angiographic contrast medium, introduction of percutaneous puncture technique, and routine use of bilateral carotid angiography built the basis for wider diagnosing of IAs. Bilateral angiography was seldom performed before 1948 [26], and routine postoperative angiography controls were started in 1952 [206]. According to af Björkesten, the direct intracranial attack became the method of choice for treating IAs in 1952 [23]. Between 1936 and 1958, 320 patients with angiographically and/or intraoperatively verified IAs were treated at the Neurosurgery Department in Helsinki [23–25,205]. Of these, 291 (91%) were diagnosed after 1951 [206]. From the hospital's operative records started in 1951 (the earlier volumes have unfortunately been lost or destroyed) we can see that although during the first year (1951) there were only three surgeries for IAs, the numbers started to rise steadily, with eight surgeries in 1952, 12 in 1953, 29 in 1954, and 30 in 1955. Most of these operations were performed by Snellman, Mäkelä and af Björkesten. The aneurysms were usually occluded directly with either linen thread ligature (42%) or silver clips (39%) (spring clips were not introduced until the 1960s) [206]. The remaining aneurysms were wrapped, trapped, treated with ICA or proximal ACA occlusion, or, infrequently, only explored. Surgical mortality between 1936 to 1958 was 9% [206]. From the very start of aneurysm surgery in Finland, the results were actively reported in international journals (Table 1), and this practice has continued ever since.

2.2.4.5. Microneurosurgery and endovascular surgery

The first neurosurgeon to use the operating microscope in Finland was Tapio Törmä in Turku in the beginning of the 1970s (personal communication J Hernesniemi). The first operating microscope at the Neurosurgery Department in Helsinki was acquired in 1974, after a delay of one year due the university financial services who considered the item a very expensive and unnecessary piece of equipment [406]. Initially, the microscope was used by neurosurgeons operating on aneurysms, small meningeomas, and acoustic schwannomas. Since laboratory training in microsurgical techniques was not deemed necessary, they usually started the use directly in the OR. A Turkish born neurosurgeon Davut Tovi from Umeå held a laboratory course in Helsinki in January 1975, during which he also demonstrated the use of microscope in the OR while the intraoperative scene was being displayed on a TV monitor (personal communication J. Hernesniemi). Interestingly, during the first years of microneurosurgery on aneurysms, intraoperative rupture often compelled the neurosurgeon to abandon the microscope and move back to macrosurgery so that he could "see better" the rupture site. But the younger generation was already starting with microsurgical laboratory training; among them Juha Hernesniemi who after his first aneurysm surgery in 1976 has performed more than 3150 aneurysm operations, all of them using a microscope. A year after visiting Yaşargil in Zürich in 1982, Hernesniemi became the first neurosurgeon in Finland to use a counterbalanced microscope equipped with a mouth switch (personal communication J. Hernesniemi). Surgery on unruptured aneurysms in patients with previous SAH started in 1979 [116], and the first paper on aneurysm surgery in patients with only incidental, unruptured aneurysms was published in 1987 [118]. Endovascular treatment of IAs began in 1991 (personal communication M. Porras).

2.3. Microsurgical anatomy for DACA aneurysms

2.3.1. Anterior cerebral artery

The ACA, the smaller of the two terminal branches of the ICA, arises at the medial end of the Sylvian fissure lateral to the optic chiasm. It traverses the optic chiasm or the optic nerve, and ascends in front of the lamina terminalis in the lamina terminalis cistern. Before entering the interhemispheric fissure, it is connected to the opposite ACA via the anterior communicating artery (ACoA) (Fig. 1). Inside the interhemispheric fissure, the left and right ACA trunks run parallel along the corpus callosum, in the pericallosal cistern. Both trunks give origin to several cortical, subcortical, and callosal branches, some of which may cross over to the opposite side. Cortical branches of the ACA supply the anterior two thirds of the medial aspects of the cerebral hemisphere as well as the superior portions of the superior frontal, precentral, and postcentral gyri [294].

The ACA is divided into five segments (A1–A5) according to Fischer (Fig. 1)[79]. The A1 segment is located between the ICA bifurcation and the ACoA. The A2 segment extends from the ACoA to the region between the rostrum and the genu of the corpus callosum (GCC). The A3 segment curves around the GCC and ends at the rostral part of the body of the corpus callosum. The A4 and A5 segments follow the superior surface of the corpus callosum with a virtual plane of division at the level of the coronary suture. Traditionally, the ACA has been divided into a proximal part (A1) and a distal part (A2 to A5), the latter also called the pericallosal artery [97,162,178,294,417,445].

2.3.1.1. A1 segment of ACA

The A1 segment arises from the ICA in the carotid cistern, and with a medial and somewhat anterior course it enters the cistern of the lamina terminalis. At this point, the A1 segment is encased by thick arachnoid bands that extend from the olfactory triangle to the lateral side of the optic nerve. When mobilizing the A1 segment, these bands require careful dissection, especially when toughened by previous SAHs. The course of the A1 segment varies in length and dominance, and it may loop under the frontal lobe [340,442]. Importantly, one A1 is dominant over the other in the majority of cases [442]. The A1s join the ACoA complex mostly above the chiasm (70%), less frequently above the optic nerves (30%) [324].

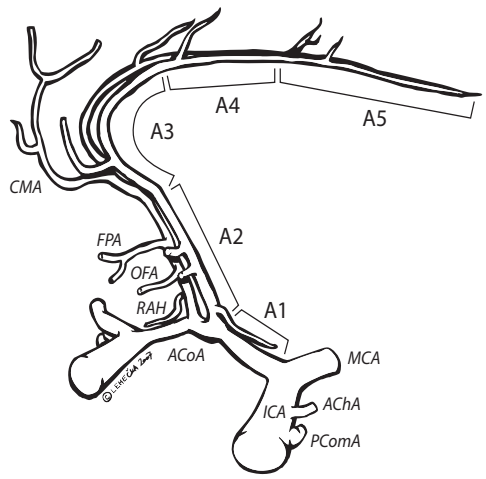


Fig. 1. *The segments (A1 to A5) and branches of the anterior cerebral artery (ACA).*

2.3.1.2. Anterior communicating artery (ACoA) complex

The ACoA is the fundamental anastomotic part of the anterior circle of Willis. Detailed microneurosurgical anatomy of the ACoA complex and its anatomic variations are reported by Yaşargil [442] and others [11,67,78,97,166,232, 295,324,327,362,392,412]. The location and orientation of the ACoA complex varies highly with respect to the optic chiasm and the anterior skull base, depending on the diameters, lengths, and courses of the A1s [295,324,442]. In 30 brains studied by Serizawa et al., two (6%)

ACoAs were high above the optic chiasm [362]. The length, shape, and diameter of the ACoA also vary [295,324,442]. The average diameters of ACoAs and A1s were 1.6 mm and 2.6 mm, respectively, in a series of 50 cadavers, and the average length of the ACoA was between 2 and 3 mm (range 0.3–7.0 mm) [295]. In cross sections, ACoAs can be round, triangular, or even almost flat. The diameter of the A1–A2 junctions was of the same size in 74%, larger in the right side in 14%, and larger in the left side in 12% [295].

2.3.1.3. Perforating branches of ACoA

It is difficult to overestimate the importance of the perforators of the ACoA complex region. The complex microneurosurgical anatomy of the perforating branches arising from the ACoA complex has been described in detail [11,12,67, 198,232,295,324,362,392,415,423,442]. Their supply areas, laterality, pattern of origin, and number vary a great deal [67,119,232,295,362, 415,423,442]. Most of them originate, like the ACoA aneurysms, from the side of the dominant A1 in case of unequal A1s, and from the medial part of ACoA with equal A1s [442]. Importantly, the perforators usually arise from the superior or posterior surface of the ACoA, rarely from its anterior or inferior surface [295]. Perforators may arise from multiple, fenestrated, or even hypoplastic and anomalous branches of the ACoAs [12,232,362,423,442]. The ACoA perforators supply the infundibulum of the pituitary, optic chiasm and superior part of the optic nerve, anterior hypothalamus and lamina terminalis, anterior perforating substance, rostrum and genu of the corpus callosum, anterior commissure, anterior cingulate gyrus, parolfactory gyrus, paraterminal gyrus, septum pellucidum, and some parts of the limbic system including the column of fornix [11,12,67,232,295,324,362,415,423, 442]. Anastomoses between some of these perforators, in particular the hypothalamic branches, are frequent [232,362].

As aneurysms of the very proximal A2 trunk may involve the perforating branches of the ACoA, they may be endangered during dissection, coagulation, application of standard or tunnel clips, or trapping procedures, especially when dealing with wide based A2As and associated arterial anomalies [232]. Impairment of these perforators during surgery may cause a wide range of neurological symptoms including memory deficits, changes in personality, and electrolyte imbalances [362,442].

2.3.1.4. A2 segment

The A2 segment originates at the junction of the A1 and the ACoA (Fig. 1). It ascends in the lamina terminalis cistern, in front of the lamina terminalis, enters the interhemispheric fissure and the callosal cistern with a course toward the

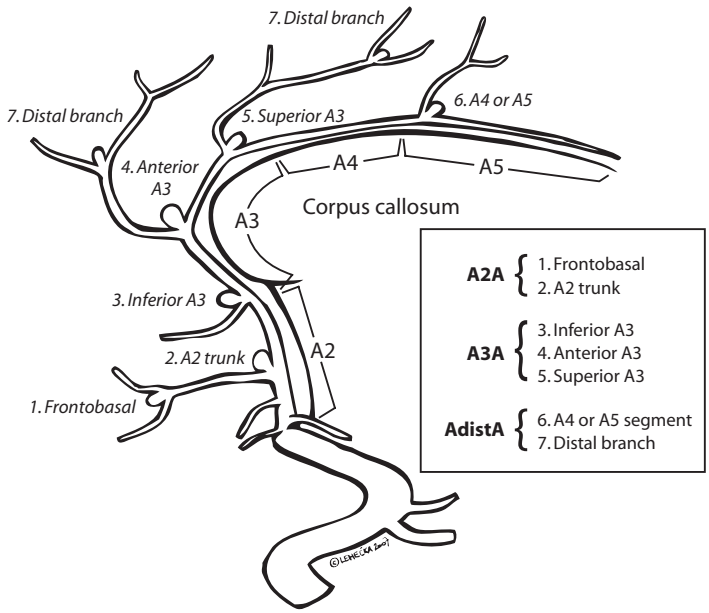


Fig. 2. *Division of DACA aneurysms according to ACA segments.*

GCC (Fig. 2). The A2 terminates at the junction of the rostrum and the genu of the corpus callosum where the A3 segment starts [294,442]. Inside the interhemispheric fissure, A2s have been seen side by side in 18% (Fig. 3a), the left A2 anteriorly in 48%, and the right A2 anteriorly in 34% [295]. The free margin of the anterior falx is well above the corpus callosum. The A2 segment is entirely below the free margin which allows free shift and crossover of its branches across the midline [294]. This means that both A2 segments can be reached via a unilateral approach [122,443].

2.3.1.5. Arterial branches of A2 segment

The A2 segment gives rise to three major branches: the recurrent artery of Heubner (RAH), the orbitofrontal artery (OFA), and the frontopolar artery (FPA) (Fig. 1). These arteries can be distinguished by their final destination but not by their diameters. High variation in the origin and size of these branches makes it impossible to define a standard vascular pattern for the A2s [178,294,417].

2.3.1.6. Recurrent artery of Heubner (RAH)

The origin of the RAH and its course in relation to the A1 trunk is highly variable. In the majority of cases, it originates from the first few mm of the A2 segment or the A1–A2 junction, and in only about 10% from the distal A1 segment [13,67,96,166,295,412,442,444]. Rare origin from the orbitofrontal branch is also known [96]. The RAH supplies the anterior inferior striatum, anterior limb of the internal capsule, olfactory region, anterior hypothalamus (overlapping with medial lenticulostriate arteries (MLAs) from A1), frontobasal cortex, and subcortical white matter [67,96,289,295,392,442]. The RAH has been found to be missing in 3% and duplicated in 12% in a series of 60 hemispheres [96]. The diameter varies a lot (0.2–2.9 mm), and in rare cases the RAH is as thick as the A1 [295]. Independent of its point of origin, the RAH directs immediately backward towards the A1 segment, and then follows the superior wall, the anterior wall, or the posterior wall of the A1 trunk. In case of the superior course (61%), the first few mm of the RAH are often attached to the A1 trunk by arachnoid bands, and their differentiation is of great importance before temporary clipping of A1 [96]. The distal part of the RAH travels freely in the subarachnoid space before penetrating into the brain at the base of the lateral and medial olfactory stria, with a highly variable branching

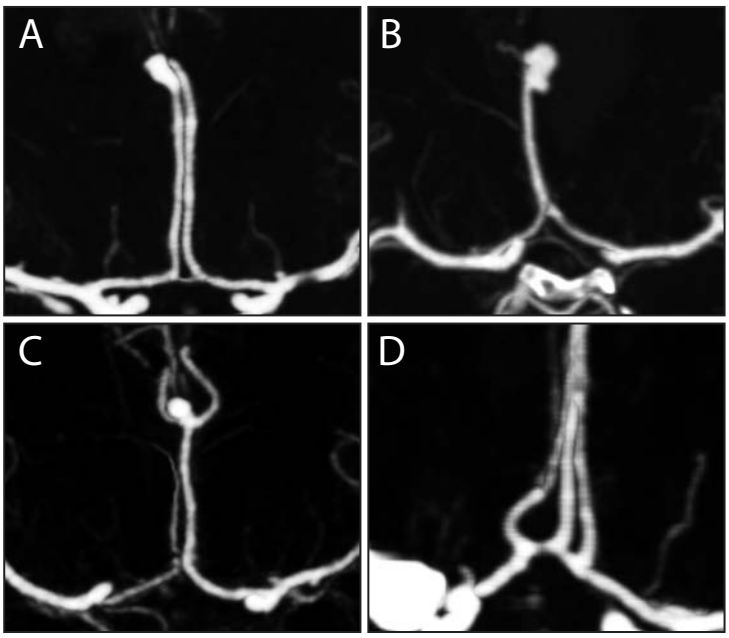


Fig. 3. *Anomalies of ACA arising from the ACoA: (**A**) Normal configuration of A2s; (**B**) Azygos ACA; (**C**) Bihemispheric ACA; (**D**) Triplicated ACA.*

pattern (1–12 branches) [67,96,295,442]. These perforators are often of the same caliber as the lenticulostriate arteries [11]. Consequently, it is very important to preserve the RAH to avoid ischemic injury to the anterior perforating substance.

2.3.1.7. Orbitofrontal artery (OFA)

The OFA arises more distally on the A2 than the RAH (Fig. 1). It generally courses downward and forward toward the floor of the anterior cranial fossa to reach the level of the planum sphenoidale. It supplies the gyrus rectus, olfactory bulb and tract, and the medial part of the orbital surface of the frontal lobe [178,294,417].

2.3.1.8. Frontopolar artery (FPA)

The FPA arises after the OFA and courses anteriorly towards the medial subfrontal surface and the frontal pole (Fig. 1). It crosses the subfrontal sulcus and supplies portions of the medial and lateral surfaces of the frontal pole [324]. It is directed anteriorly rather than laterally which helps to distinguish it from the RAH. Both the OFA and the FPA can be identified in over 95% of hemispheres [417]. They do not always arise from the A2 trunk but may also arise from the A1 trunk or even the callosomarginal artery (CMA) [162,178,324,417].

2.3.1.9. Basal perforating branches

A2 gives also rise to small basal perforating branches which overlap the ACoA perforators. These A2 perforators are usually four in number and they supply the anterior hypothalamus, septum pellucidum, medial portion of the anterior commissure, pillars of the fornix, and anteroinferior part of the striatum [294,295]. They pass posteriorly to enter the optic chiasm, lamina terminalis, and anterior forebrain below the corpus callosum [294]. The medial portions of the rostrum and the genu of the corpus callosum are mainly supplied by the subcallosal artery which arises from the ACoA [415].

2.3.1.10. A3 segment and its branches

The A3 segment starts at the junction of the rostrum and the genu of the corpus callosum, curves around the genu, and terminates at the origin of the horizontal part of the ACA [79] (Fig. 2). All A3 to A5 segments coursed in the callosal sulcus in 60%, at least one segment was found in the cingulate sulcus in 33%, and in 7% the A3 to A5 segments were located in the cingulate sulcus, not involving the corpus callosum at all [415]. The A3 segment gives origin to several cortical branches: the anterior internal frontal artery (AIFA); the middle internal frontal artery (MIFA); the posterior internal frontal artery (PIFA); and most importantly, the CMA [294]. High variation in the origin and size of these branches makes it impossible to define a standard vascular pattern for the A3s [178,294,417]. Some of the cortical branches may have a common trunk of origin, may arise from different segments, or may be totally absent [178,294,417]. The three internal frontal arteries (see above) supply the medial and lateral surfaces of the superior frontal gyrus as far posteriorly as the paracentral lobule [324]. In addition to the cortical branches, there are also thin arteries originating from the A3 to A5 segments which directly supply the superficial surface of the corpus callosum, called callosal and cingulocallosal arteries [415].

2.3.1.11. Callosomarginal artery (CMA)

The CMA is the major branch of the distal ACA with diameter of 1.8–1.9 mm, as thick as the ACA at the same level [294,417]. Like other cortical branches of the ACA, the CMA cannot be defined by its branches since the usual branches of that region can arise directly from the ACA trunk as well. The CMA has been defined as the artery that courses in or near the cingulate sulcus and gives rise to two or more

major cortical branches [257]. The CMA is totally absent in 9–18% [162,178,294,417]. It originates most frequently (73%) at the A3 (Fig. 1), but origins from the A2 or the A4 were also observed [294]. After its origin, the CMA courses in or near the cingulate sulcus and often gives rise to several cortical branches. According to the course, three types of hemispheres have been described: 1) no CMA; 2) atypical CMA, lacking the long course in the cingulate sulcus and oriented directly toward the cortex (Fig. 4a); and 3) typical CMA, running parallel to the pericallosal artery in the cingulate sulcus for a relatively long distance (Fig. 4b) [417]. The origin of the CMA is the most frequent site for the DACA aneurysms [52,122,279,312,383].

2.3.1.12. A4 and A5 segments and their cortical branches

The A4 segment begins at the horizontal portion of the ACA and continues backward along the superior surface of the corpus callosum towards the splenium (Fig. 1). The virtual plane of division between the A4 and the A5 segments is the coronary suture. The most important branches originating from the A4 and A5 segments are: the posterior internal frontal artery (PIFA), the paracentral artery, the superior parietal artery, and the inferior parietal artery [294,324]. The PIFA originates as often from the A3 segment as the A4 segment. High variation in the origin and diameter makes it impossible to consistently classify the cortical branches of the A3 to A5 segments of the ACA [178,294,417]. The cortical branches of the A4 and the A5 usually supply the posterior third of the superior frontal gyrus, part of the cingulate gyrus, a portion of the premotor, motor, and somatic sensory areas, the precuneus, and adjacent portions of the cuneus [324].

2.3.1.13. Anatomic anomalies of ACA

The important anomalies involving the ACA are: azygos ACA; bihemispheric ACA; triplication of ACA; and crossover branches of the ACA [14,97,198,216,294,442]. The azygos ACA is a single trunk distal to the A1 segments, so it supplies both hemispheres (Fig. 3b). In the bihemispheric ACA, one A2 is hypoplastic and the larger A2 gives origin to most of the cortical branches (Fig. 3c). In case of ACA triplication (Fig. 3d), the middle A2, also called the hemispheric type of the medial callosal artery [415], is prominent and supplies the corpus callosum. Crossover branches, found in 26–64% of patients, originate from the distal ACA and continue to the contralateral hemisphere where they supply a small medial area [294,380]. Severing of the crossover branches may cause injury to the contralateral side of the approach. In anatomic studies, the azygos ACA was seen in 0.2–4%, the bihemispheric ACA in 0.2–12%,

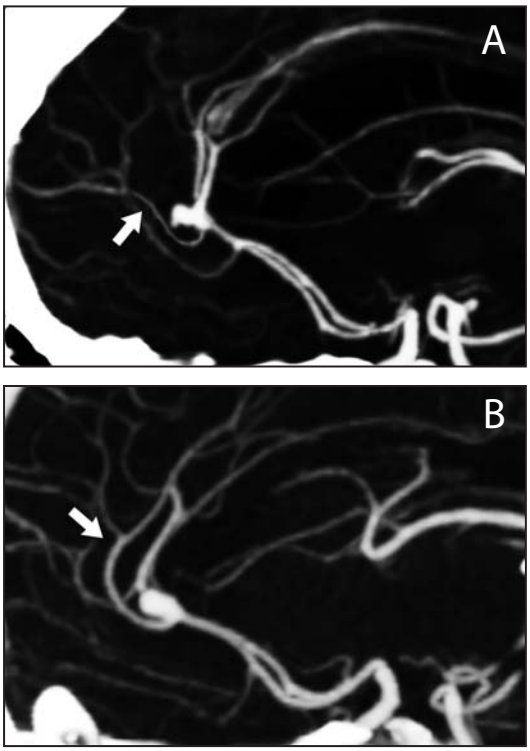


Fig. 4. *(**A**) Atypical course of the callosomarginal artery (CMA) directly towards the cortex. (**B**) Typical course of the CMA in the cingulate sulcus.*

and the triplication of ACA in 3–13% of patients [14,97,178,216,294,380,416,417,442].

2.3.2. Interhemispheric fissure

DACA aneurysms are located in the midline, inside the interhemispheric fissure, where the cerebral hemispheres are partially separated by the falx. The depth of the falx varies, but its free margin is well above the corpus callosum. Importantly, the A2, A3 and A4 segments are usually below the free margin which allows free shift and crossover of their branches across the midline [294]. On the other hand, only the most anterior portions of the A5 segment and the CMA are bellow the free margin. The cingulate gyri may be so adherent to each other that during the surgical exposure they may be mistaken for the corpus callosum [443]. The interhemispheric fissure is narrow and only a limited amount of cerebrospinal fluid (CSF) can be removed from there.

2.3.3. Venous structures

The frontal superficial veins are divided into three groups: lateral, medial, and inferior. In addition, each group comprises a group of ascending and a group of descending veins [280]. The veins draining the lateral convexity of the frontal lobe are either ascending to the superior sagittal sinus or descending to the superior sylvian vein. The ascending veins are frontopolar, anterior frontal, middle frontal, posterior frontal, precentral, and central veins [280,323]. The ascending veins of the medial frontal surface join the ascending convexity veins along the superior rim of the frontal lobe to form subdural bridging veins that empty into the superior sagittal sinus [178,280,293,323,367]. The descending veins of the medial surface drain the genu and the rostrum of the corpus callosum, and an adjacent part of the cingulate gyrus. They terminate in the inferior sagittal sinus or into the anterior cerebral vein, which joins the deep sylvian vein [323].

The bridging veins, with a diameter of 1–4 mm, have a short free course (5–10 mm) in the subdural space before entering the superior sagittal sinus [323]. Bridging veins may enter the sagittal sinus directly, but they may also first join a meningeal sinus within the dura, with a course of 5–30 mm to the lateral angle of the sagittal sinus [8,280]. A single meningeal sinus may drain several cortical veins. The dura may also contain enlarged venous spaces called lacunae, extending laterally up to 3 cm from the midline. The lacunae predominantly drain meningeal veins before entering the sagittal sinus [280]. Most of the cortical veins pass beneath the lacunae and enter directly into the superior sagittal sinus, but a few have a common access to the sinus. The lacunae are largest in the posterior frontal region. Arachnoid granulations often protrude into the floor and walls making them adherent to the cortical surface (Fig. 5).

The bridging veins pose a potentially dangerous obstacle to the surgical approaches into

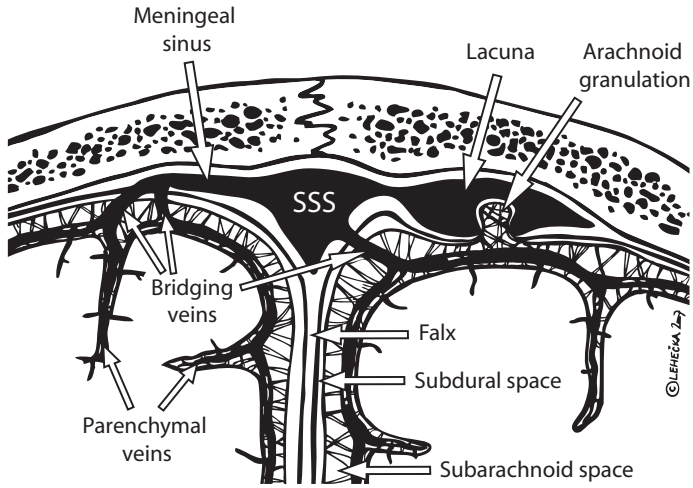


Fig. 5. *The superior sagittal sinus (SSS) and its relation to venous lacunae, meningeal sinuses, and bridging veins.*

the interhemispheric space. All bridging veins should be left intact if possible, and sufficient working space should be searched in between them. The venous pattern varies highly, but often a corridor of some centimeters can be found [280]. The larger the damaged or sacrificed vein and the closer to the central sulcus it lies, the higher the risk of venous infarction with clinical symptoms. Aplastic superior sylvian vein requires special attention because of high risk of venous infarction due to reduced venous collateral flow [293].

Inside the interhemispheric fissure, one may encounter the right and left anterior pericallosal veins side by side on the corpus callosum, varying highly in size. The pericallosal veins drain the genu and rostrum of the corpus callosum and empty into the anterior end of the inferior sagittal sinus [323]. They should be left intact if possible, but there are often good venous collaterals.

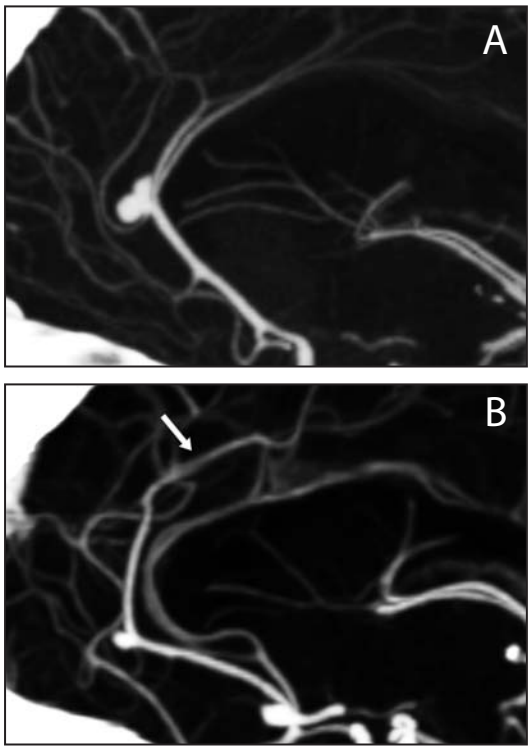


Fig. 6. *The pericallosal artery coursing: (**A**) along the corpus callosum; (**B**) in the cingulate sulcus (arrow).*

2.3.4. Corpus callosum

The corpus callosum is the major transverse commissure connecting the cerebral hemispheres. It is divided into rostrum, genu, body, and splenium [396,415]. The rostrum and the genu form a connection between the anterior portion of the frontal lobes and comprise the floor and the anterior wall of the frontal horn of the lateral ventricle. The body connects the posterior portion of the frontal lobes and the parietal lobes and forms the roof of the lateral ventricles. The splenium is the most posterior part of the corpus callosum and it connects regions of the temporal and occipital lobes. The genu of the corpus callosum is semicircular or oval in the sagittal section with a mean anteroposterior diameter of 11 mm [178]. The anterior portion of the corpus callosum gets its blood supply from the ACA and the splenium is supplied by the posterior cerebral artery (PCA). The callosal, cingulocallosal, and long callosal arteries originating from the pericallosal artery supply directly the superficial surface of the genu and the body of the corpus callosum and the cingulate gyrus [162,415].

The pericallosal artery (A2 to A5 segments) travels along the corpus callosum for the majority of its course (Fig. 2). It makes a wide arch around the GCC (A3 segment) and then runs posteriorly along the superior aspect of the corpus callosum (Fig. 6a). Türe et al. reported an irregular course in almost 40% so that at least one of the A3 to A5 segments coursed in the cingulate sulcus instead of the callosal sulcus (Fig. 6b) [415]. During microsurgery the corpus callosum can be identified by its white color and parallel running transverse fibers [370]. One of the most common mistakes during interhemispheric approach is to confuse the tightly attached cingulate gyri for the corpus callosum which can lead to total loss of orientation inside the interhemipheric fissure.

2.4. Distal anterior cerebral artery aneurysms

2.4.1. Incidence and location of DACA aneurysms

DACA aneurysms, also referred to as pericallosal artery aneurysms, are located distally to the ACoA on the A2–A5 segments of the anterior cerebral artery (ACA) and its branches (Fig. 1)[198]. They are relatively rare, comprising about 6% (range 2–9%) of all IAs [52,122,142, 205,248,279,312,368,383,438,445,449]. DACA aneurysms are further divided into subgroups based on their exact locations with respect to the segments of the ACA and the corpus callosum.

2.4.1.1. Aneurysms of the ACA

Aneurysms of the ACA can be classified into five different groups: aneurysms of the A1 segment or proximal anterior cerebral artery aneurysms (A1As); anterior communicating artery aneurysms (ACoAAs); aneurysms of the A2 segment and its frontobasal branches or proximal pericallosal aneurysms (A2As); aneurysms of the A3 segment or classical pericallosal aneurysms (A3As); and aneurysms of the A4 and A5 segments and distal cortical branches or distal pericallosal aneurysms (AdistAs) (Table 2, Fig. 2) [47]. The last three groups represent the DACA aneurysms.

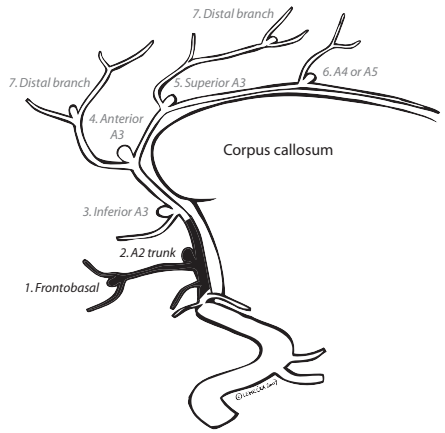


Fig. 7. *Proximal DACA aneurysms (A2As).*

2.4.1.2. A2As (Proximal pericallosal aneurysms)

A2As are located either directly on the pericallosal artery, between the ACoA and the genu of the corpus callosum (A2 segment), or on one of its frontobasal branches (Fig. 7). Proximal pericallosal artery aneurysms (A2As) are rare. The reported incidence of A2As has been 0.2–1% of all IAs or about 5–22% of all DACA aneurysms [52,122,142,205,248,279,311,368,383, 438,445,449]. They are frequently involved with perforating arteries arising from both the ACoA and the A2 segment, as well as arterial anomalies of this region [14,294,433].

Table 2. *The five classification categories of ACA aneurysms.*

Category	Location
A1A	A1 segment, between ICA bifurcation and ACoA
ACoAA	Anterior communicating artery
A2A	A2 segment and its frontobasal branches, between ACoA and genu of corpus callosum
A3A	A3 segment, curving around genu of corpus callosum
AdistA	A4 and A5 segments or distal cortical branches such as CMA

CMA: Callosomarginal artery

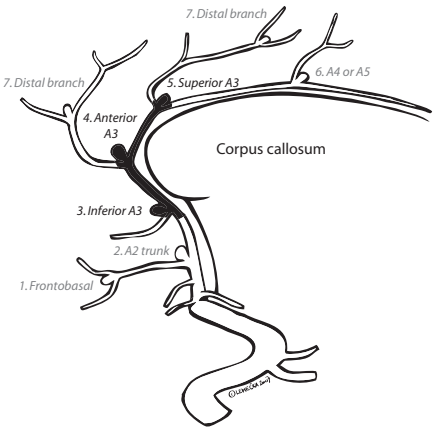


Fig. 8. *Classical DACA aneurysms (A3As).*

2.4.1.3. A3As (Classical pericallosal aneurysms)

A3As are located at the A3 segment of the ACA at the GCC, often at the origin of the CMA (Fig. 8). They have also been called pericallosal artery–callosomarginal artery junction aneurysms or "loco classico" pericallosal artery aneurysms. A3As are the most common of the DACA aneurysms. Their incidence is 2–7% of all IAs or 69–82% of all DACA aneurysms [52,122,142,205, 248,279,311,368,383,438,445, 449]. A3As are difficult to reach as they lie deep in the interhemispheric fissure closely attached to the surrounding brain.

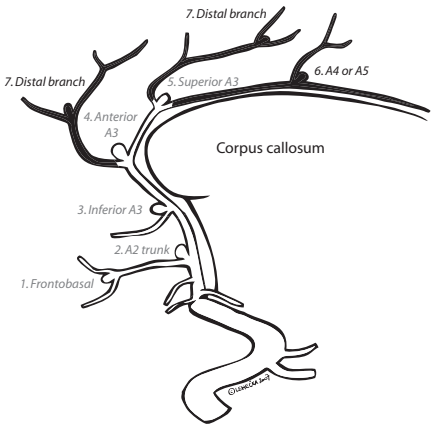


Fig. 9. *Distal DACA aneurysms (AdistAs).*

2.4.1.4. AdistAs (Distal pericallosal aneurysms)

AdistAs are located at the A4 and the A5 segments of the ACA, distal to the GCC, or on the cortical branches that originate from the A3 to A5 segments, e.g., the CMA (Fig. 9). AdistAs are the least frequent of all DACA aneurysms with an incidence of only 0.3–0.6% of all IAs or 5–20% of all DACA aneurysms [52,122,311,368, 383,449].

2.4.2. Clinical symptoms

When DACA aneurysms rupture, they usually present with the same symptoms as seen in other ruptured aneurysms, i.e. headache, nausea, and loss of consciousness depending on the amount of bleeding [383]. Still, there are some unique neurological deficits which are more often seen in this aneurysm group, including akinetic mutism, bilateral leg weakness, behavioral changes and cognitive deficits [33,71,87,99,382]. These findings are thought to be related to bilateral damage to the vascular territory supplied by the distal ACA, especially the bilateral cingulate gyri and other limbic structures, and the supplementary motor area (SMA), caused either by mass effect after ICHs, or infarction [33,343].

2.4.3. Anatomic features

2.4.3.1. Size

DACA aneurysms are small; even when ruptured their mean size varies from 5 to 8 mm [32, 52,122,245,264,279,368,383]. This is somewhat less than for aneurysms located more proximal to the circle of Willis [31]. The small size of DACA aneurysms is thought to relate to Laplace's law, which states that the wall tension required to withstand a given pressure increases with the diameter of the vessel [31]. In addition, DACA aneurysms have often a broad base with possible neck calcifications and originating branches

nearby [52,122,205,248,279,312,368, 383,438,443,449].

2.4.3.2. Multiple aneurysms

DACA aneurysms are often associated with other aneurysms [52,122,279, 312,443,449]. Associated aneurysms have been reported in 25% to 55% of patients with DACA aneurysms [52, 122,142,279,312,368,376,383,438, 443], which is higher than the usual 28–35% reported for other aneurysm locations [49,50,70,140,331].

2.4.3.3. ICH and IVH

DACA aneurysms tend to bleed into the adjacent brain tissue causing ICH in 17–73% of the patients [122,172, 231,312,368,376,383]. The highest density of blood in the subarachnoid space is in the distal interhemispheric fissure, pericallosal cistern, and lamina terminalis cistern [384]. The ICH is usually located in the frontal lobe, corpus callosum or cingulate gyrus (Fig. 10)[143]. The high incidence of ICHs, higher than for aneurysms elsewhere, is obviously related to the narrow pericallosal cistern and the dense attachments to the adjacent brain surface [47,312]. IVH is seen in 25–30% of the patients (Fig. 10a), more frequently related to ruptured A2As and A3As than AdistAs [47]. Frontal ICHs are likely to cause late cognitive deficits [382].

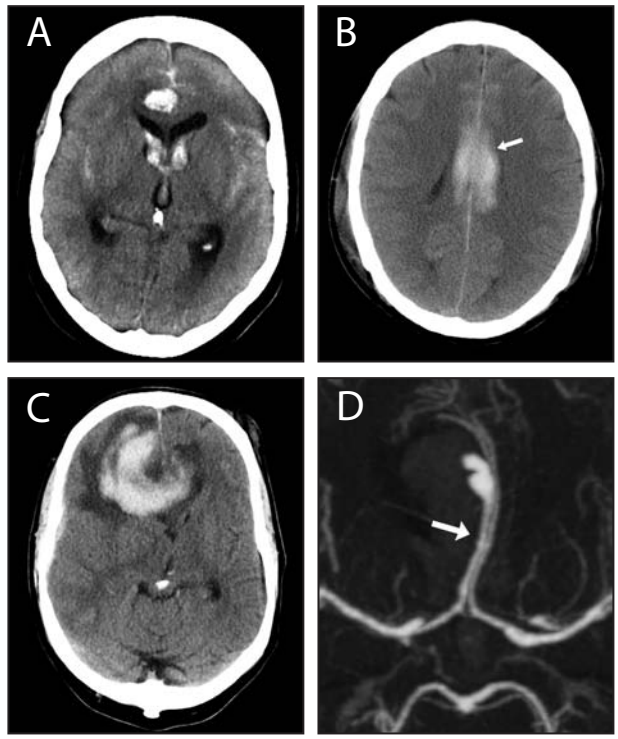


Fig. 10. *(**A**) ICH with IVH component related to ruptured DACA aneurysm. (**B**) ICH located above the corpus callosum as seen often in ruptured AdistAs (arrow). (**C**) Expansive frontal ICH due to ruptured A3A. (**D**) Dislocation of the pericallosal arteries (arrow) due to the ICH.*

2.4.3.4. Association with ACA anomalies

DACA aneurysms are often associated with various anomalies of the ACA [122,383,438], which are thought to cause greater blood flow and shear stress on the vessel wall, and thus increase the susceptibility to aneurysm formation at the bi-, tri-, and quadrifurcations of these arteries [10,266]. Huber et al. reported an association between anomalies of the ACA and DACA aneurysms in an angiographic series [133]. In anatomic autopsy studies of patients without aneurysms, the azygos ACA was seen in 0.2–4%, the bihemispheric ACA in 0.2–12% and the triplication of ACA in 3–13% of patients [14,97,178, 216,294,380,416,417,442]. However, in clinical series, different anomalies of the ACA have been observed in 7–35% of patients with DACA aneurysms, an incidence generally higher than in the autopsy studies [32,142,205,383,443]. Most of the clinical observations on this association between different ACA anomalies and DACA aneurysms are based on case reports, and of these most have described the azygos ACA [399].

2.4.3.5. Association with AVMs

In addition to ACA anomalies, DACA aneurysms are thought to be associated with cerebral arteriovenous malformations (AVMs) [122,383,438]. AVMs have been reported in 3–15% of DACA aneurysm patients [52,205,383,438].

2.4.4. Special subgroups of DACA aneurysms

2.4.4.1. Giant DACA aneurysms

Giant DACA aneurysms (diameter ≥ 25 mm) are extremely rare. So far, there have been only 29 cases reported in the literature (Table 3). Only few of them were reported as part of a larger series on DACA aneurysms [52,56,122,248,376,383], most as case reports [21,74,113,114,164,197, 226,247,269,285,299,308,310,365,372,399,414, 440]. Since giant DACA aneurysms may mimic the symptoms of frontal tumors, MRI and DSA are essential for reaching a correct diagnosis [215,378]. CT and CTA are helpful in identifying calcifications at the aneurysm base.

2.4.4.2. Aneurysms associated with azygos ACA

As mentioned earlier (see 2.4.3.4.) DACA aneurysms are frequently associated with anomalies of the ACA. Of such anomalies, the azygos ACA (Fig. 3b) has received the most attention. In larger series on DACA aneurysms, an azygos ACA has been observed in 3–22% of patients [16,32,52,142,177,188,202,205,248,264,273, 276,279,376,383]. In addition, there exists a large number of case reports on the subject (Table 4). It seems that the incidence of azygos ACAs compared to bihemispheric ACAs in connection with DACA aneurysms has been overestimated. It is actually very difficult to distinguish between these two anomalies in the normal DSA, even with compression of the contralateral carotid artery [14,176]. CTA or rotational DSA give more accurate information for making the distinction between the two anomalies.

Table 3. *Published cases of giant DACA aneurysms.*

Authors	Year	No. of giant DACA aneurysms
Snyckers and Drake [376]	1973	1
O'Neill et al. [285]	1979	1
Pia and Zierski [299]	1979	1
Pozzati et al. [308]	1982	1
Smith and Parent [372]	1982	1
Hayashi et al. [114]	1985	2
Yamagami et al. [440]	1986	1
Nitta et al. [269]	1987	1
Maiuri et al. [226]	1990	1
Mishima et al. [247]	1990	1
Hashizume et al. [113]	1992	1
Hernesniemi et al. [122]	1992	1
Preul et al. [310]	1992	1
Shiokawa et al. [365]	1993	2
Farias et al. [74]	1997	1
deSousa et al. [52]	1999	2
Kanemoto et al. [164]	2000	1
Koyama et al. [197]	2000	1
Miyazawa et al. [248]	2000	1
Türe et al. [414]	2001	1
Topsakal et al. [399]	2003	1
Biondi, et al. [21]	2006	2
Dinc et al. [56]	2006	1
Steven et al. [383]	2007	2
Present series		(1+1)*
Total number		**30**

*One of the two cases was previously reported already in Hernesniemi et al. 1992 series.

2.4.4.3. Traumatic DACA aneurysms

Aneurysms of traumatic origin represent less than 1% of all IAs [19,172,261] and traumatic DACA aneurysms are even more rare [142]. Traumatic DACA aneurysms have been

Table 4. *Published cases of DACA aneurysms associated with azygos ACA.*

Author	Year	Series/ Case report	No. cases
Laitinen and Snellman [205]	1960	Series	3
Pool and Potts [305]	1965	Series	3
Handa et al. [108]	1971	Case report	1
Snyckers and Drake [376]	1973	Series	1
Kinoshita and Matsukado [188]	1975	Series	2
Quencer and Cox [313]	1977	Case report	1
Fankhauser and Zander [73]	1978	Case report	1
Katz et al. [176]	1978	Case report	1
Nukui and Aiba [273]	1978	Series	2
Becker and Newton [16]	1979	Series	1
Kessler [183]	1979	Case report	1
Kondo et al. [195]	1979	Case report	1
Huber et al. [133]	1980	Case report	7
Olbert et al. [282]	1980	Case report	1
Fujimoto et al. [90]	1981	Case report	1
Niizuma et al. [266]	1981	Case report	2
Fukawa et al. [92]	1982	Case report	1
Benedetti and Curri [18]	1983	Case report	1
Kuwabara et al. [202]	1984	Series	3
Abe et al. [1]	1985	Case report	2
Hayashi et al. [114]	1985	Case report	2
Kaneko et al. [163]	1985	Case report	7
Kobayashi et al. [192]	1986	Case report	1
Yamagami et al. [440]	1986	Case report	1
Harada et al. [109]	1987	Case report	1
Ogasawara et al. [276]	1987	Series	4
Kawamura et al. [177]	1988	Series	6
Lightfoote et al. [217]	1989	Case report	1
Schick et al. [352]	1989	Case report	1
Mishima et al. [247]	1990	Case report	1
Nardi et al. [262]	1990	Case report	2
Ohno et al. [279]	1990	Series	3
Calzolari et al. [30]	1991	Case report	1
Cinnamon et al. [34]	1992	Case report	1
Hashizume et al. [113]	1992	Case report	1
Traynelis et al. [404]	1992	Case report	1
Zderkiewicz et al. [452]	1992	Case report	1
Shiokawa et al. [365]	1993	Case report	1
Baykal et al. [15]	1996	Case report	2
Inci et al. [142]	1998	Series	1
Ng et al. [264]	1998	Series	3
Suzuki et al. [391]	1998	Case report	1
deSousa et al. [52]	1999	Series	2
Dietrich et al. [55]	2000	Case report	1
Kanemoto et al. [164]	2000	Case report	1
Miyazawa et al. [248]	2000	Series	9
Topsakal et al. [399]	2003	Case report	1
Auguste et al. [10]	2004	Case report	4
Fujimoto et al. [91]	2004	Case report	1
Chhabra et al. [32]	2005	Series	3
Hussain et al. [137]	2005	Case report	5
Huh et al. [134]	2007	Case report	3
Jagetia et al. [146]	2007	Case report	1
Steven et al. [383]	2007	Series	6
Present series			4
Total number			**120**

described in only some case reports (Table 5). They are typically found in young patients or children [209–211,359,450]. The pericallosal artery is thought to be prone for formation of traumatic aneurysms after a head trauma, since the lower margin of the falx may directly damage the arterial wall of the pericallosal artery [450]. Traumatic DACA aneurysms are usually fusiform, with thin walls and poorly defined necks [37], which makes their treatment very challenging. Wrapping, proximal occlusion, excision, trapping, parent artery occlusion with preoperative bypass, and reconstruction can be considered for these aneurysms [17,187,208,347]. Sometimes even a preoperative bypass, side-to-side A3–A3 bypass or arterial translation (e.g. STA-ACA) is needed [179,185,186,212,294].

2.4.5. Imaging of DACA aneurysms

Digital subtraction angiography (DSA) is still the valid gold standard in many centers [237]. Recently, multislice helical CT-angiography (CTA) has begun to replace DSA as a noninvasive, safe, and quick imaging method with sensitivity and specificity comparable to DSA in aneurysms larger than 2 mm [98,165,167,292,366, 397,422,434,435]. In addition, it allows disclosure of calcifications in the arterial walls and quick reconstruction of 3D images [174]. In giant or partially thrombosed DACA aneurysms, MRI is valuable for evaluating the presence and extension of intraluminal thrombus. Nowadays, 3T magnetic resonance angiography (MRA) shows good potential in iden-

Table 5. *Published cases of traumatic DACA aneurysms.*

Author	Year	No. cases
Raimondi et al. [318]	1968	1
Umebayashi et al. [418]	1970	1
Acosta et al. [2]	1972	1
Ferry and Kempe [77]	1972	1
Benoit and Wortzman [19]	1973	1
Sadar et al. [346]	1973	1
Thompson et al. [395]	1973	3
Endo et al. [72]	1974	1
Amacher et al. [5]	1975	1
Fleischer et al. [83]	1975	1
Berger et al. [20]	1976	1
Sarwar et al. [349]	1976	1
Asari et al. [9]	1977	1
Laurent et al. [211]	1981	1
Jakobsson et al. [147]	1984	2
Nov and Cromwell [272]	1984	2
Amagasa et al. [6]	1986	4
Martin and Hummelgard [233]	1986	1
Nakstad et al. [261]	1986	3
Yuge et al. [450]	1990	1
Senegor [359]	1991	1
Opeskin [286]	1995	1
Raju et al. [319]	2001	1
Lath et al. [210]	2002	1
Cohen et al. [37]	2005	2
Dunn et al. [68]	2007	1
Steven et al. [383]	2007	3
Present series		1
Total number		**40**

tifying small details of the vasculature without the side effects of radiation [4,227].

2.4.6. Treatment of DACA aneurysms

2.4.6.1. History

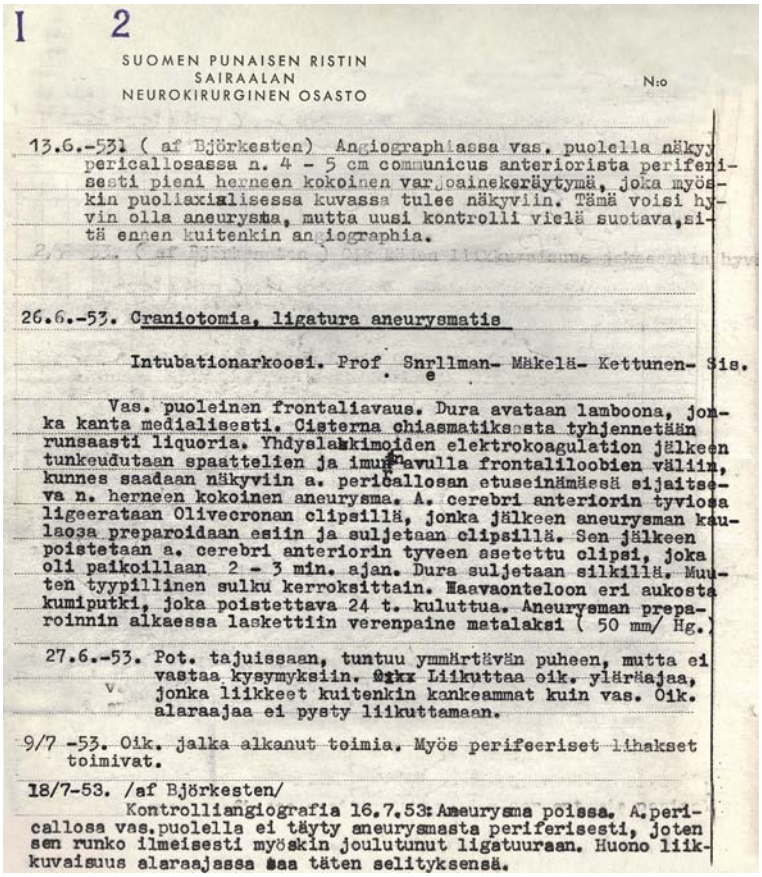
In 1948, Sugar and Tinsley were the first to perform intracranial surgery for a DACA aneurysm in a 19-year old girl [386]. Not being able to locate the aneurysm during the operation, they decided to occlude the parent pericallosal artery. The patient survived the procedure, but developed left-sided hemiparesis.

The first intracranial surgery for a DACA aneurysm in Finland was performed on June 26th, 1953 by Aarno Snellman on a 51-year old woman with a ruptured left-sided DACA aneurysm at the A3 segment [205]. The aneurysm was clipped at the neck with Olivecrona's clip four months after the initial rupture. Transcript of the operation report is shown in Fig. 11. An interesting detail is the use of Olivecrona's clip on the parent artery for the purpose of temporary clipping. Postoperatively, the patient developed right-sided hemiparesis, and angiography showed occlusion of the distal part of the left pericallosal artery, which was probably accidentally left within the clip. The patient recovered from the hemiparesis and eventually was able to cope independently with her daily household chores. After her unfortunate death two years later, no autopsy was performed, but the death certificate stated intracranial hemorrhage as the cause of death.

In 1954, Wilson et al. published an autopsy series of 143 patients who died of SAH [433]. Ruptured DACA aneurysms were the cause of death in seven (5%) of them, giving the first estimate of the incidence of DACA aneurysms. Later studies have shown this to be a fairly accurate figure [52,122].

2.4.6.2. Conservative treatment

Conservative treatment of DACA aneurysms has a very poor prognosis. Already the first reports on DACA aneurysms, with small patient numbers, showed high mortality (50–100%) in the conservatively treated group [81,205,244]. The largest series on conservative treatment of ruptured DACA aneurysms, the Cooperative Study of Intracranial Aneurysms in 1966, reported mortality rate as high as 75% at one year follow-up [267]. This result was far worse than for any other aneurysm location. In the same study, the mortality rate for surgically treated DACA aneurysm patients was 32% [371], which was also relatively high compared to the mortality rates of 15-25% in the previous reports



I 2

SUOMEN PUNAISEN RISTIN
SAIRAALAN
NEUROKIRURGINEN OSASTO

N:o

13.6.-53 (af Björkesten) Angiographiassa vas. puolella näkyy pericallosassa n. 4 - 5 cm communicus anteriorista perifer-isesti pieni herneen kokoinen varjoainekeräytymä, joka myös-kin puoliaxialisessa kuvassa tulee näkyviin. Tämä voisi hy-vin olla aneurysma, mutta uusi kontrolli vielä suotava, si-tä ennen kuitenkin angiographia.

26.6.-53. Craniotomia, ligatura aneurysmatis

Intubationarkoosi. Prof. Snellman- Mäkelä- Kettunen- Sis.

Vas. puoleinen frontaliavaus. Dura avataan lamboona, jon-ka kanta medialisesti. Cisterna chiasmatiksesta tyhjennetään runsaasti liquoria. Yhdyslakkimoiden elektrokoagulation jälkeen tunkeudutaan spaattelien ja imun avulla frontaliloobien väliin, kunnes saadaan näkyviin a. pericallosan etuseinämässä sijaitse-va n. herneen kokoinen aneurysma. A. cerebri anteriorin tyviosa ligeerataan Olivecronan clipsillä, jonka jälkeen aneurysman kau-laosa preparoidaan esiin ja suljetaan clipsillä. Sen jälkeen poistetaan a. cerebri anteriorin tyveen asetettu clipsi, joka oli paikoillaan 2 - 3 min. ajan. Dura suljetaan silkillä. Muu-ten tyypillinen sulku kerroksittain. Haavaonteloon eri aukosta kumiputki, joka poistettava 24 t. kuluttua. Aneurysman prepa-roinnin alkaessa laskettiin verenpaine matalaksi (50 mm/ Hg.)

27.6.-53. Pot. tajuissaan, tuntuu ymmärtävän puheen, mutta ei vastaa kysymyksiin. Liikuttaa oik. ylärajaa, jonka liikkeet kuitenkin kankeammat kuin vas. Oik. alaraajaa ei pysty liikuttamaan.

9/7 -53. Oik. jalka alkanut toimia. Myös perifeeriset lihakset toimivat.

18/7-53. /af Björkesten/
Kontrolliangiografia 16.7.53: Aneurysma poissa. A. peri-callosa vas. puolella ei täyty aneurysmasta periferisesti, joten sen runko ilmeisesti myöskin joulutunut ligatuuraan. Huono liik-kuvaisuus alaraajassa saa täten selityksensä.

Fig. 11. *Transcript of the operation report from the first DACA aneurysm surgery performed in Finland on 26th June 1953. Translation of the report (original in Finnish):*

"The Finnish Red Cross Hospital, Neurosurgical Ward

13th June 1953. (af Björkesten) On angiography, a collection of contrast medium of the size of a small pea is seen on the left pericallosal artery about 4–5 cm distally from the anterior communicating artery. This can be seen also on half-axial image. This could well be an aneurysm, but repeat control should be made. First, however, the patient should undergo angiography.

26th June 1953. Craniotomia, ligatura aneurysmatis
Intubation anesthesia. Prof. Snellman-Mäkelä-Kettunen-Nurse
Left-sided, frontal craniotomy. Dura is opened as a single flap with the base medially. Significant amount of CSF is released from chiasmatic cistern. After electrocoagulation of the bridging veins the interhemispheric space in between the frontal lobes is entered with spatulas and suction until the aneurysm of the size of a pea is visualized on the anterior wall of the left pericallosal artery. The basal part of the anterior cerebral artery is dissected and ligated with Olivecrona's clip. The base of the aneurysm is dissected free and closed with a clip. The clip at the base on the anterior cerebral artery is then removed. It was in place for 2–3 min. Dura is closed with silk. Otherwise typical closure in layers. Rubber tube is inserted under the wound through a separate opening, it should be removed after 24 hours. At the beginning of the aneurysm dissection the blood pressure was lowered (50 mm/Hg).

27th June 1953. The patient is conscious, she seems to understand what is spoken but does not answer questions. She moves her right arm, but this is clumsier than the left one. She cannot move the right leg.

9th July 1953. The right leg has started to function. Also the peripheral muscles function.

18th July 1953 (af Björkesten) Control angiography 16th July 1953: Aneurysm is gone. The left-sided pericallosal artery does not fill distally from the aneurysm. So it seems that it is also trapped inside the clip. The poor movement of the lower limb is thus explained."

on DACA aneurysms [81,107,205,244,305]. Nevertheless, after the Cooperative Study, conservative treatment has not been considered to be an option for patients with ruptured DACA aneurysms unless they are initially in a very poor clinical condition.

2.4.6.3. Direct surgery before microneurosurgery

The aneurysm series by McKissock and Walsh (1956), and Hamilton and Falconer (1959) both included DACA aneurysms as a separate group, containing seven and six patients, respectively [107,244]. In both of these series, DACA aneurysms were considered to be a rarity of only minor clinical importance, but at the same time they were thought to be difficult to be operated on.

The first aneurysm series dedicated to DACA aneurysms came from Laitinen and Snellman in Finland in 1960 [205]. They described their experience with 14 patients, of whom 10 were treated by direct surgery and four conservatively. Of the conservatively treated patients, two died (50% mortality), whereas in the surgically treated group there was only one death (10% mortality). Aneurysm occlusion was achieved either by ligating the neck with linen thread or by using silver clips. Several important features of DACA aneurysms are noted by the authors. They realized that DACA aneurysms are frequently associated with multiple aneurysms and anomalies of the ACA, and that they are firmly attached either to the falx or the cingulate gyri. In their evaluation of the surgical technique they found that the interhemispheric approach is much more suitable than the subfrontal approach for reaching the DACA aneurysms. They also noted the general difficulties in proper visualization of the aneurysm base in the deep and narrow interhemispheric fissure. In one of their patients, the aneurysm clip accidentally occluded the contralateral pericallosal artery.

Other reports on the treatment of DACA aneurysms in a small number of patients followed (Table 6) [81,305,432]. The Cooperative Study of Intracranial Aneurysms in 1966 had the largest number of DACA aneurysms at that time, with 26 conservatively and 39 surgically treated DACA aneurysms [371]. The mortality of 32% in this series was rather high, but it was still slightly lower than the mortality rates for patients with aneurysms in other locations. This was the first indication that patients with ruptured DACA aneurysms may have a slightly better outcome than patients with aneurysms elsewhere.

In 1979, Yoshimoto and Suzuki presented their series of 34 DACA aneurysms operated without the operating microscope, with an exceptionally low 3% mortality [449]. In this paper, the DACA aneurysms are divided into three groups based on the aneurysm's exact location with respect to the corpus callosum, and the authors discuss the differences in approaches to each of these locations. This paper remains the last one to report results without the use of the operating microscope.

2.4.6.4. Microneurosurgery for DACA aneurysms

Introduction of microneurosurgery was a great advance in the treatment of DACA aneurysms. Suddenly it was possible to obtain a much better visualization of both the aneurysm and the adjacent vascular structures, which meant safer and more accurate occlusion of the aneurysm base. The first report on microneurosurgical management of DACA aneurysms came from Yaşargil and Carter in 1974 [445]. The report describes 13 consecutive patients operated on by Yaşargil who started to use an operating microscope and microneurosurgical techniques in 1967. There were no deaths related to the surgery itself, but one patient died a few months later from new SAH, this time caused by a previously unrecognized, ruptured MCA aneurysm. The general microneurosurgical technique for treatment of DACA aneurysms described in this paper is very similar to the one still in use. The major advances over time are related to better preoperative imaging, refined instruments, and certain microneurosurgical

Table 6. *Series on treatment of DACA aneurysms published before 2008.*

Author(s)	Year	No. cases	Clipped	Coiled	Indirect surgery	Conservative
Before microneurosurgery						
McKissock and Walsh [244]	1956	7	4	0	1	2
Hamilton et al. [107]	1959	6	3	0	3	0
Laitinen and Snellman [205]	1960	14	9	0	1	4
Pool and Potts [305]	1965	3	2		1	0
Wilson et al. [432]	1965	4	4	0	0	0
Fisher and Ciminello [81]	1966	4	3	0	0	1
Skultety and Nishioka [371]	1966	65	27	0	12	26
Dechaume et al. [53]	1973	12	6	0	0	6
Snyckers and Drake [376]	1973	24	15	0	0	9
Kinoshita and Matsukado [188]	1975	10	8	0	0	2
Nukui and Aiba [273]	1978	26	22	0	0	4
Becker and Newton [16]	1979	12	9	0	0	3
Yoshimoto et al. [449]	1979	34	34	0	0	0
Microneurosurgery						
Yaşargil and Carter [445]	1974	13	13	0	0	0
Kuwabara et al. [202]	1984	18	17	0	0	1
Mann et al. [231]	1984	11	11	0	0	0
Yaşargil [443]	1984	23	23	0	0	0
Ogasawara et al. [276]	1987	18	12	0	0	6
Wisoff and Flamm [438]	1987	20	20	0	0	0
Kawamura et al. [177]	1988	29	20	0	0	9
Sindou et al. [368]	1988	19	16	0	0	3
Ohno et al. [279]	1990	42	34	0	0	8
Fukushima et al. [93]	1991	26	26	0	0	0
Hernesniemi et al. [122]	1992	84	67	0	0	17
Martines et al. [234]	1996	11	11	0	0	0
Proust et al. [312]	1997	43	43	0	0	0
Inci, et al. [142]	1998	14	14	0	0	0
Ng et al. [264]	1998	30	25	0	0	5
deSousa, et al. [52]	1999	72	72	0	0	0
Miyazawa et al. [248]	2000	54	54	0	0	0
Chhabra et al. [32]	2005	28	28	0	0	0
Dinc et al. [56]	2006	26	24	1	0	1
Oshiro et al. [288]	2007	20	20	0	0	0
Steven et al. [383]	2007	59	58	1	0	0
Endovascular						
Pierot et al. [300]	1996	8	0	8	0	0
Menovsky et al. [245]	2002	12	0	12	0	0
Keston et al. [184]	2004	18	0	17	0	1
Nguyen, et al. [265]	2007	26	0	25	0	1
Pandey et al. [291]	2007	41	13	28	0	0
Present series		501	405	17	8	71

technical nuances developed over the years by Yaşargil and others [52,122,279,443].

In the following years, a number of reports were published on microneurosurgical management of DACA aneurysms (Table 6). The fact that most of these series are small with less than 30 patients [32,56,93,142,177,202,231,234,264, 276,288,368,438,443] shows how infrequent DACA aneurysms are and how difficult it is to obtain experience in their treatment even at one institution.

In 1990, Ohno et al. published the first of the larger DACA aneurysm series with 42 consecutive patients showing only a 2% surgical mortality [279]. Based on Yaşargil's reports [443,445], it was already evident that with microneurosurgery the mortality rates would be much lower than before, and that more focus was needed on morbidity analysis and efforts to identify patients with good or poor prognosis. Patients, divided into groups based on the Hunt and Hess classification [135], had to be evaluated separately. Ohno et al. reported good outcome in 92% of the Grade I and II patients [279]. In addition, they noted that DACA aneurysms are generally small, 94% being ≤10mm.

In 1992, Hernesniemi et al. from Kuopio Finland, published the largest series to date on DACA aneurysms [122]. They had 84 consecutive patients with 92 DACA aneurysms, of which 65 were ruptured. The main strength of this series lies in the relatively unselected patient population with only 40% of the patients initially in Grade I and II. The management mortality of 19% reflects the high number of Grade IV and V patients in the material and cannot be well compared with the highly selected previous series. On the other hand, 96% of the Grade I and II patients had favorable outcomes. These results were based on early surgery (within 72 hours) in the acute SAH phase. This paper also presents frontobasal aneurysms as a special subgroup of DACA aneurysms for the first time.

Proust et al. presented an analysis of 43 patients with DACA aneurysms, 35 of them ruptured, in 1997 [312]. They had a favorable outcome in 66% of the patients, but this was affected by the large number (26%) of Grade IV and V patients. They concluded that the skill of the neurosurgeon is the key for successful DACA aneurysm surgery.

In 1999, deSousa et al. published a large series of 72 DACA aneurysms treated with microneurosurgery [52]. This series is highly selected, as almost all of the patients were operated on more than 10 days after SAH and there was only one Grade IV and V patient. Surgical mortality was 7% and 85% of the patients had a good outcome. Unlike in the previous series, the authors did not report the correlation between preoperative grade and outcome, but this was probably due to the patient selection and delayed surgery. However, they made an interesting observation that patients who underwent clipping of multiple aneurysms through several different approaches during the same operation had worse outcomes than those on whom only a single approach was used. This finding is in agreement with other authors with regard to the treatment of multiple aneurysms in general, possibly due to the increased risk of vasospasm [330].

Miyazawa et al. published a statistical analysis of factors affecting the outcome of DACA aneurysms in microsurgically treated patients in 2000 [248]. Their multivariate analysis showed that the preoperative grade and delayed timing of surgery were the only factors which affected the surgical outcome. This analysis did not include patients treated conservatively or any Grade V patients. Furthermore, the patient population (n=52) was small compared to the number of variables tested (n=13) which may have affected the results.

The most recent series on microneurosurgical treatment of DACA aneurysms was published by Steven et al. in 2007 [383]. Of the 59 patients, 36 had ruptured DACA aneurysms with a 17% management mortality and 58% favorable outcome. Based on univariate analysis, the authors identified the clinical grade and presence or absence of ICH as the factors affecting outcome in patients with ruptured DACA aneurysms.

2.4.6.5. Technical difficulties in DACA aneurysm surgery

Microsurgical clipping of DACA aneurysms presents certain specific difficulties when compared to other aneurysm locations as previously described by several authors [52,122,142, 231,248,264,279,312,383,438,443,445]. Yaşargil listed these special features related to DACA aneurysms: 1) lack of working space in the interhemispheric space and pericallosal cistern; 2) dense adhesions between the cingulate gyri make separation and finding of the aneurysm difficult; 3) sclerotic wall and broad base of the aneurysm require precise positioning of the aneurysm clip; 4) origins of the branching arteries at the neck and attachment of the dome to the opposite pericallosal artery increase the risk of vascular ischemic complications; 5) difficulty in identifying lateralization of the parent artery from the preoperative images; 6) attachment or embedding of the dome in the pial layer of the cingulate gyrus increases the risk of tear in the aneurysm wall during dissection; and 7) with aneurysm at the bifurcation of an azygos pericallosal artery, complications may lead to vascular damage of both hemispheres [443].

Most DACA aneurysms are operated via the anterior interhemispheric route [441,443]. Some authors have used the bifrontal basal anterior interhemispheric approach [32,390]. Partial resection of the genu of the corpus callosum to enlarge the exposure in the infracallosal region is not advisable as it may lead to neuropsychological deficits [181]. Using the anterior interhemispheric approach, the aneurysm dome and the possible rupture site are encountered before appropriate proximal control has been achieved. This together with the dense attachments to the surrounding brain tissue are thought to result in frequent intraoperative ruptures of DACA aneurysms in 19–50% of the cases [122,142,248,312,376, 383].

2.4.6.6. Endovascular treatment

Clipping has been the gold standard treatment for DACA aneurysms for the past decades. However, since the first report on endovascular treatment of DACA aneurysm by Pierot et al. in 1996 [300], the number of coiled DACA aneurysms has been increasing although not to an extent comparable to other aneurysm locations. As with surgical treatment, the published series have been rather small so far (Table 6). Coiling is considered to be more demanding for DACA aneurysms than for most other aneurysms, and thereby also the complication rate has been higher [184,265,300]. Pierot et al. reported that only two of eight DACA aneurysms could be successfully coiled [300]. Keston et al. reported three (18%) ruptures during coiling of 17 DACA aneurysms, and satisfactory initial packing was obtained in 14/17 (82%) [184]. Nguyen et al. reported three (12%) perforations in their series of 25 DACA aneurysms, one perforation causing hemorrhage resulting in transient hemiparesis, dyslexia and acalculia [265]. During the mean follow-up of 28 months, they saw aneurysm recurrence in 53% of the patients, but there were no rebleeds. On the other hand, in all of these series, patients with SAH had a similar outcome as in most surgical series [184,245,265,291]. Pandey et al. attempted to compare the treatment results between clipping and coiling of DACA aneurysms in their series comprising 13 clipped and 28 coiled patients [291]. There was, however, a strong selection bias in the two groups which prevented any definite conclusions. Clipping and coiling were likewise compared in the International Subarachnoid Aneurysm Trial (ISAT), which included a relatively large number of DACA aneurysms (95 out of 2143 aneurysms), but due to the weakness of the subgroup post hoc analysis, no information on the possible superiority of either treatment was provided [251].

2.4.6.7. Technical difficulties in coiling of DACA aneurysms

It seems that, using the present technology, endovascular occlusion of DACA aneurysms is demanding because of their small size, relatively wide neck, branches originating close to the base, small caliber of the parent artery, and distal location of the aneurysm [184,245,265,291]. DACA aneurysms are difficult to reach via small diameter parent arteries and there is often a lack of stability and support for optimal coil deployment. Suboptimal initial coiling results easily in aneurysm recurrence [265]. As with microsurgical treatment, the result of the endovascular treatment depends very much on the experience of the surgeon, and the selection of treatment should be accordingly evaluated independently for each case. Only a long-term follow-up will indicate what is the durability of coiling in DACA aneurysms.

2.4.7. Outcome

2.4.7.1. Short-term outcome

Microsurgical series of patients with ruptured DACA aneurysms have reported favorable outcomes in 58–83% and management mortality in 7–21%, respectively [52,122,231,264,279,312, 368,383,438]. The results vary depending on how selected the patient material is, what is the timing of the surgery, and whether the short-term outcome is evaluated at discharge or later e.g. at one year. Some authors have suspected a less favorable prognosis for patients with DACA aneurysms compared to other aneurysm sites [52,231]. In other series, the outcome has been similar to that of other aneurysm locations, e.g. in the ISAT with only 11% of patients initially in Grade III to V, favorable outcome at one year was seen in 73% of the patients and mortality was 9% [250]. In general, mortality due to ruptured DACA aneurysms is unlikely to be higher than for aneurysms at other locations, but cognitive problems due to frontal lobe injury are more often encountered [122,382].

2.4.7.2. Predictors of short-term outcome

Only few studies have evaluated factors affecting the short-term outcome in patients with DACA aneurysms [248,291,383]. All of them have identified the initial Hunt and Hess grade as the most important factor in both univariate and multivariate analysis. A larger aneurysm size and the presence of an ICH are also expected to affect the outcome [248,383]. Old age, which has been shown to correlate with less favorable outcome in SAH patients in general [207,287,329,342], seems to predict less favorable outcome also in patients with DACA aneurysms [291].

2.4.7.3. Long-term outcome

Relatively little is known about the long-term survival after aneurysmal SAH as only two population based studies have been published [281,337]. Major studies such as the ISAT and ISUIA reported outcomes after a mean follow-up of four years [251,431], other studies even earlier after the initial rupture [105,131]. There is no data available on the long-term outcome of patients with DACA aneurysms. One theory is that, since DACA aneurysms are located relatively distally in the cerebrovascular tree with narrow parent arteries, they might experience smaller shear stress onto the aneurysm wall making them less prone to rebleed after treatment than aneurysms at more proximal locations [427].

3. Aims of the study

I. To determine the distribution of DACA aneurysms along the different segments of distal anterior cerebral artery, and to evaluate vascular anomalies of this region.

II. To study the short-term management outcome of DACA aneurysms and to evaluate the variables influencing the outcome.

III. To assess the long-term outcome and excess-mortality in patients with ruptured DACA aneurysm compared with the normal Finnish population.

IV.–VI. To describe the present techniques in microneurosurgical management of DACA aneurysms at different locations:

IV. A2 segment of the anterior cerebral artery and the frontobasal branches (A2As)

V. A3 segment of the anterior cerebral artery (A3As)

VI. A4 and A5 segments of the anterior cerebral artery and the distal cortical branches (AdistAs)

4. Patients, materials and methods

This study is based on the retrospective data of 517 patients who were treated for DACA aneurysm between 1936 and 2007 at two Finnish neurosurgical units with population responsibility for the whole Southern Finland (Helsinki University Central Hospital) and Eastern Finland (Kuopio University Hospital). The combined catchment area of these two departments consists of close to 3 million people. Each part of the study (I to VI) included a subgroup of the whole study population (Table 7).

4.1. Publication I: Anatomic features of DACA aneurysms

4.1.1. Patients and images

Publication I is based on the 101 consecutive patients diagnosed with DACA aneurysm between 1998 and 2007 at the neurosurgical unit in Helsinki. The DACA aneurysms were identi-

Table 7. *Basic characteristics of each subgroup of the patient population in the different parts (I to VI) of this study.*

Characteristic	Part I	Part IIa*	Part IIb†	Part III	Part IV-VI
Center(s)	Helsinki	Helsinki+Kuopio	Helsinki+Kuopio	Helsinki+Kuopio	Kuopio
Time period	1998-2007	1936-1979	1980-2005	1976-2003	1977-2005
No. patients	101	74	427	280	215
Sex					
Male (%)	27 (27%)	44 (59%)	170 (40%)	119 (43%)	104 (48%)
Female (%)	74 (73%)	30 (41%)	257 (60%)	161 (57%)%	111 (52%)
Age [years]; mean (range)	53 (17–80)	40 (4–59)	51 (14–80)	50 (14–80)	52 (22–77)
No. DACA aneurysms (%)	108	79	470	304	235
Ruptured	67 (62%)	68 (86%)	277 (59%)	280 (92%)	128 (54%)
Unruptured	41 (28%)	11 (14%)	193 (41%)	24 (8%)	107 (46%)
Aneurysm location (%)					
A2A	7 (6%)	20 (25%)	59 (13%)	48 (16%)	35 (15%)
A3A	90 (83%)	57 (72%)	377 (80%)	239 (79%)	174 (74%)
AdistA	11 (11%)	2 (3%)	34 (7%)	17 (5%)	26 (11%)
Aneurysm size[mm]; median (range)	6 (1–35)	7 (3–50)	6 (1–41)	6 (2–41)	5 (1–40)
Hunt&Hess grade, no (%)					
I-II	—‡	43 (59%)	132 (31%)	140 (50%)	66 (31%)
III	—	21 (28%)	88 (21%)	88 (31%)	41 (19%)
IV-V	—	4 (5%)	57 (13%)	52 (19%)	21 (10%)
DACA Unruptured	—	6 (8%)	150 (35%)	0 (0%)	87 (40%)

* The historical series from 1936 to 1979 before CT and routine microneurosurgery

† From 1980 to 2005, microneurosurgery and CT routinely available

‡ Not evaluated

fied either by conventional DSA (Integris V3000 1024×1024 matrix; Philips Medical Systems, Best, The Netherlands) in 39 (39%) patients, or more recently by CTA (GE Lightspeed QX/i; GE Medical Systems, Milwaukee, WI, USA) in 62 (61%) patients. The use of routine CTA started in year 2000 and has since become the primary imaging modality for cerebral aneurysms at this institution [165,191]. Four-vessel angiography was performed in 93 (92%) patients, eight (8%) patients had only carotid angiography.

4.1.2. Image analysis

All radiological data were analyzed in digital form by an experienced neurovascular radiologist (Matti Porras). All aneurysms and associated AVMs were identified in each patient. The ruptured and unruptured DACA aneurysms were divided according to their location. For each DACA aneurysm we measured the maximum dome length, maximum dome width, neck width, diameter of the parent artery, and the distance from the ACoA complex along the pericallosal artery (Fig. 12). The aneurysm dome and base with all the originating branches were evaluated. We identified anomalies of the ACA (azygos ACA, bihemispheric ACA, and triplicated ACA) in each patient. The course, dominancy, and origin of the branches from the pericallosal artery harboring the DACA aneurysm were evaluated.

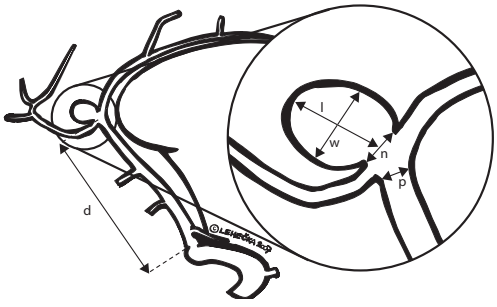


Fig. 12. *Measurements from angiograms: l=dome length, w=dome width, n=neck width, p=parent ar-tery diameter, d=distance from ACoA along the pericallosal artery (in mm).*

4.1.3. Statistical analysis

The data were analyzed using SPSS for Windows, version 13.0.1 2004 (SPSS, Inc., Chicago, IL, USA). Categorical variables were compared using the Fisher exact two-tailed test, Pearson chi-square test, or the test for linear trend. Continuous variables were compared between groups with the Mann-Whitney U-test or the t-test.

4.2. Publication II: Treatment and outcome of DACA aneurysms

4.2.1. Patients

Publication II presents the combined experience of Helsinki and Kuopio neurosurgical units in the treatment of DACA aneurysms in a consecutive, retrospective series of 427 patients with 470 DACA aneurysms treated during the years 1980 to 2005, the era of routine CT imaging and microsurgery (*Part b*). In addition, a historical data of 74 patients treated before year 1980 is evaluated separately for the results of premicroneurosurgical era (*Part a*).

The 427 patients from years 1980 to 2005 were divided into three groups: (1) 277 patients with primary SAH from a ruptured DACA aneurysm; (2) 94 patients with unruptured DACA aneurysm(s) and without acute SAH or SAH sufficiently long time ago (median 4 months) from another aneurysm; and (3) 56 patients with unruptured DACA aneurysm(s) with acute SAH from another aneurysm. We focused on the DACA aneurysm patients treated with microsurgery (n=362) but those few treated

with endovascular occlusion (n=17) were analyzed as well. Patients described previously by Hernesniemi et al. in 1992 were reanalyzed in the present series [122].

The 277 patients with a primary rupture from a DACA aneurysm (Group 1) were compared to the 2243 consecutive patients from 1980 to 2005 with primary SAH from any ruptured aneurysm in the Kuopio Cerebral Aneurysm Database. The Kuopio Cerebral Aneurysm Database contains information about all the aneurysm patients treated from year 1977 onward at the Department of Neurosurgery, Kuopio University Hospital [47–50,119].

4.2.2. Data collection

Patients' clinical charts and radiological data were reviewed for relevant information. DACA aneurysms were identified by conventional DSA or recently by CTA [165]. SAH was diagnosed with CT (n=261) or by lumbar puncture (n=16). The initial clinical condition was graded with the Hunt and Hess (H&H) grading system [135].

Follow-up data were collected from the day of diagnosis of a DACA aneurysm until death or December 31st, 2006. Vital status at the end of the year 2006 was ascertained from the Population Register Centre which contains information on all individuals residing in Finland. Dates and causes of death were obtained from the Statistics Finland. Outcome at one year was assessed by the Glasgow Outcome Score (GOS) [152], and further classified as favorable (GOS≥4) or unfavorable (GOS<4). The 427 patients had a total follow-up time of 3398 patient years, with a median of 7 years (range 0–24 years). No patients were lost to follow-up.

4.2.3. Statistical analysis

The data were analyzed using SPSS for Windows, version 13.0.1 2004 (SPSS, Inc., Chicago, IL, USA). Categorical variables were compared using the Fisher exact two-tailed test, Pearson chi-square test, or the test for linear trend. Continuous variables were compared between groups with the Mann-Whitney U-test or the t-test. Univariate association of continuous variables was tested using Spearman rank correlation coefficients.

For the 277 patients with primary SAH from a ruptured DACA aneurysm, risk factors for unfavorable outcome (GOS<4) at one year were analyzed using unconditional logistic regression by estimating the univariate and multivariate odds ratios (OR) with 95% confidence intervals (CI). The tested variables and their distribution are shown in Table 8. The maximum-likelihood stepwise forward and backward elimination procedures were used, with

Table 8. *Test variables used for logistic regression analysis of unfavorable outcome after SAH from ruptured DACA aneurysm (n=277) and their distribution.*

Tested variable	Distribution
Age [years]*	51 (14–80)
Sex; male	110/277
Treatment time period [year]*	1994 (1980–2005)
Hypertension	88/274
Cardiac disease	33/271
Hunt&Hess grade ≥ 3	145/277
Aneurysm size [mm]*	6 (2–41)
Aneurysm location at A_3 segment	224/277
Associated aneurysms	96/277
Fisher grade ≥ 3	214/261
ICH	137/261
IVH	90/261
Severe pre-op hydrocephalus	23/261
Re-bleeding before treatment	53/274
Delay in treatment [days]*	2 (0–105)
Treatment of multiple aneurysms in same session	19/277
Use of temporary occlusion	44/161
Intraoperative aneurysm rupture	57/268
Ventricular drainage	37/277
Permanent shunt	28/277

* For continuos variable given as mean (range)

selection of variables based on the magnitude of their probability values (<0.1). A two-tailed probability value less than 0.05 was considered significant.

4.3. Publication III: Long-term outcome of ruptured DACA aneurysms

4.3.1. Patients

In publication III we followed retrospectively the 280 consecutive patients who were treated in Helsinki and Kuopio neurosurgical units for ruptured DACA aneurysms in 1976–2003. Diagnosis of SAH was based on lumbar puncture before 1980 and on CT thereafter. Ruptured DACA aneurysms were identified either by DSA or recently by CTA. Clinical status on admission was expressed by the Hunt and Hess scale [135].

4.3.2. Follow-up

The follow-up data were collected starting from the day of diagnosis of SAH until death or December 31st 2004. Vital status at the end of year 2004 was ascertained from the Population Register Centre which contains information on all people residing in Finland. The dates and causes of death were obtained from Statistics Finland. From the same register we also obtained causes of death for the whole population of Finland during the study period. The mean follow-up time was 9.6 years (range 0.1–29 yrs).

4.3.3. Statistical analysis

Relative survival ratio (RSR) provided a measure of the excess mortality for patients diagnosed with ruptured DACA aneurysms irrespective of whether the excess mortality was directly or indirectly attributable to the illness [69]. The RSR was calculated by dividing the observed survival rates by the expected ones. Using the Ederer II method, the expected survival was derived from that of the comparable general population of Finland matched with respect to age, sex, and calendar time based on the data from Statistics Finland [69]. The 95% confidence intervals (95%CI) for annual relative survival and cumulative relative survival estimates were calculated by assuming normal distribution. Statistical analysis was carried out using SAS software version 8.02 (SAS Institute Inc., Cary, NC, USA).

4.4. Publications IV-VI: Microneurosurgical management of DACA aneurysms

4.4.1. Patients (Kuopio Cerebral Aneurysm Database)

The data presented in publications IV to VI of this study represents 3005 consecutive patients harboring 4253 IAs from the Kuopio Cerebral Aneurysm Database (1977–2005) [47–50,119]. From this database we identified 35 patients with A2As (publication IV), 163 patients with A3As (publication V), and 26 patients with AdistAs (publication VI). Prevalence of each location was calculated and other important features related to microneurosurgical treatment of these aneurysms were identified.

4.4.2. Analysis of microneurosurgical technique

Microneurosurgical strategies for clipping of the DACA aneurysms were evaluated based

on information obtained from the previous parts of this study (publications I to III), and on careful analysis of the microneurosurgical videos made available for this study by Professor Juha Hernesniemi, Helsinki University Central Hospital. Considerations on approaches and microsurgical techniques for clipping DACA aneurysms are discussed for each location group.

4.4.3. Microneurosurgical videos

We selected and edited demonstrative videos illustrating the microneurosurgical treatment of DACA aneurysms at different locations (see section List of 12 supplementary videos on microneurosurgery of DACA aneurysms).

5. Results

5.1. Incidence of DACA aneurysms (publications IV-VI)

Of the 3005 patients in the Kuopio Cerebral Aneurysm Database, 1145 (38%) had 1179 ACA aneurysms and 215 (7%) patients had 235 DACA aneurysms. The 235 DACA aneurysms represented 6% of all the 4253 intracranial aneurysms. There were 35 patients with 35 A2As, 0.8% of all the 4253 IAs; 163 patients with 174 A3As, 4% of all the 4253 IAs; and 26 patients with 26 AdistAs, 0.6% of all the 4253 IAs. In our series, 2365 patients presented with primary SAH, in 855 (36%) of them the cause was a ruptured ACA aneurysm. Of our 35 A2As, 21 (60%) were ruptured, 0.9% of all ruptured IAs; of the 174 A3As, 97 (56%) were ruptured, 4% of all ruptured IAs; and of the 26 AdistAs, 10 (38%) were ruptured, 0.4% of all ruptured IAs.

5.2. Anatomy of DACA aneurysms (publication I)

5.2.1. Microneurosurgical classification

We classified the DACA aneurysms into seven groups with the genu of the corpus callosum as the anatomic landmark for the division (Fig. 2, Table 9). Aneurysms at each of these locations require modified microsurgical approaches. Table 9 and Fig. 13 present the distribution of the 108 DACA aneurysms (67 ruptured, 41 unruptured) according to their anatomic location. The A3 segment was the most frequent with 70 (65%) of the aneurysms anterior to the GCC, 19 (18%) aneurysms inferior, and only one (1%) aneurysm superior to the GCC (Fig. 14a-g). The remaining 18 DACA aneurysms were distributed fairly evenly between the remaining locations with the frontobasal ones the least frequent

***Table 9**. Microneurosurgical division of DACA aneurysms and their frequencies among 108 DACA aneurysms in Helsinki from 1998 to 2007.*

Name	Location	Frequnecy (%)	
		Ruptured n=67	Unruptured n=41
Frontobasal aneurysms	On the frontobasal branches originating form the A2 segment	2%	2%
A2 trunk aneurysms	Directly on the A2 segment, most often at the origin of the frontopolar artery (FPA)	4%	5%
Inferior A3 aneurysms	On the proximal part of the A3 segment inferior to the genu of corpus callosum	15%	22%
Anterior A3 aneurysms	On the central part of the A3 segment anterior to the genu of corpus callosum.	69%	59%
Superior A3 aneurysms	On the distal part of the A3 segment superior to the genu of corpus callosum	2%	0%
A4 or A5 aneurysms	On either the A4 or A5 segment	4%	10%
Distal branch aneurysms	On the distal cortical branches originating from the A3 to A5 segments such as the callosomarginal artery (CMA)	4%	2%

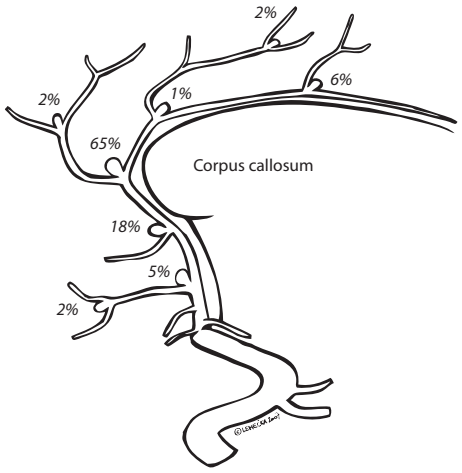


Fig. 13. *Distribution of 108 DACA aneurysms based on the microneurosurgical division.*

(2%). Rupture status of the aneurysm did not affect this distribution. There were 32 ruptured and 19 unruptured aneurysms on both the left and right sides. Six (6%) patients had either an azygos ACA or a triplicated ACA with the aneurysm in the midline. The pericallosal artery ran along the corpus callosum inside the pericallosal cistern in 97 (96%) of the 101 patients (Fig. 6a), in the remaining four (4%) patients it was found in the cingulate sulcus for at least part of its course (Fig 6b).

5.2.2. Aneurysm size

The size of the DACA aneurysm was mainly dependent on its rupture status. The ruptured ones were larger than the unruptured ones with mean maximal diameters of 7.4 mm (range 2–35 mm) and 4.2 mm (range 1–9 mm), respectively, ($p<0.001$). All size variables and measurements are presented in Table 10. Many of the aneurysms were small, 36 (54%) of the 67 ruptured ones and as many as 34 (83%) of the 41 unruptured ones were smaller than 7 mm. There was no statistical significance between the size and location in either the ruptured or the unruptured aneurysms.

5.2.3. Dome and base

The orientation of the dome was dependent on the anatomic location of the aneurysm. In the sagittal plane, most of the frontobasal, A2 trunk and inferior A3 aneurysms had their dome directed forward. The anterior A3 aneurysms had their dome pointing either forward or upward, and the aneurysms distal to the A3 segment had mainly backward projecting domes. On axial view, most of the aneurysms were in the midline, and only 26% were directed laterally.

The mean diameter of the DACA aneurysm neck was 2.6 mm (range 1–8 mm), in ruptured

Table 10. *Measurements of the 108 DACA aneurysms in ruptured and unruptured groups and their size distribution.*

	Ruptured (n=67)	Unruptured (n=41)	Total (n=108)
Length [mm]; mean±SD	7.4±4.7	4.2±2.2	6.2±4.2
Width [mm]; mean±SD	5.3±3.2	3.2±1.6	4.6±2.9
Neck [mm]; mean±SD	2.8±1.3	2.4±0.8	2.6±1.2
Parent artery diameter [mm]; mean±SD	1.8±0.4	1.7±0.5	1.8±0.4
Neck to width ratio; mean±SD	0.58±0.22	0.80±0.20	0.66±0.24
Neck to parent artery ratio; mean±SD	1.6±0.7	1.5±0.7	1.5±0.7
Size distribution			
Small (<7mm); n (%)	36 (54%)	34 (83%)	70 (65%)
Medium (7–14mm); n (%)	27 (40%)	7 (17%)	34 (31%)
Large (15–24mm); n (%)	3 (4%)	0	3 (3%)
Giant (≥25mm); n (%)	1 (2%)	0	1 (1%)

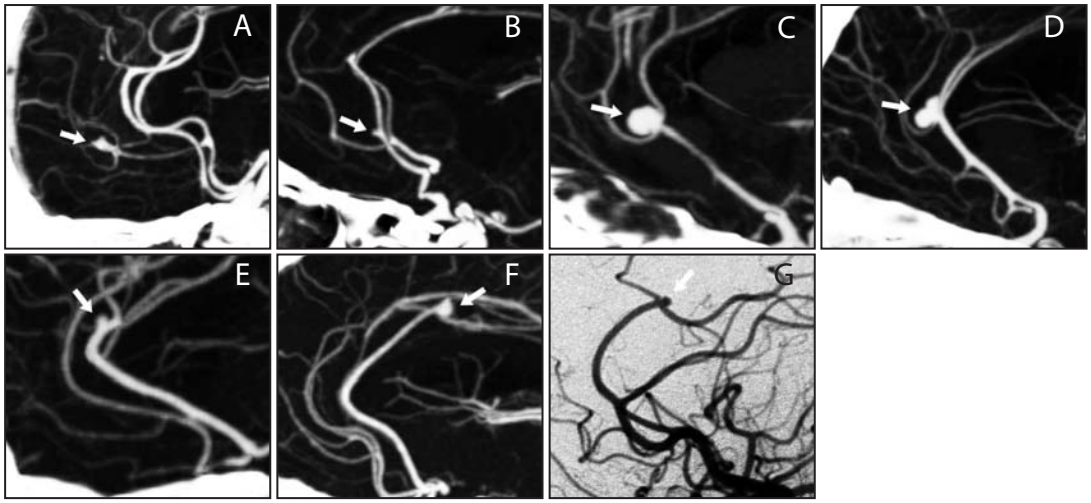


Fig. 14. *CTA and DSA images of DACA aneurysms at different locations based on microneurosurgical division, arrow marks the aneurysm; (**A**) Frontobasal, (**B**) A2 trunk, (**C**) Inferior A3 segment, (**D**) Anterior A3 segment, (**E**) Superior A3 segment, (**F**) A4 or A5 segments, (**G**) Distal branches (distal callosomarginal artery).*

ones slightly wider (0.4 mm) than in the unruptured ones (Table 10). The neck-to-width ratio was larger for the unruptured aneurysms than for the ruptured aneurysms with mean values of 0.8 (1:1.3) and 0.6 (1:1.7), respectively. In 81% of all the aneurysms the neck-to-dome ratio was more than 1:2, with 25% of them having their neck equal to the dome width (1:1). The mean parent artery diameter was 1.8 mm (range 1.0–3.0 mm) for both the ruptured and unruptured aneurysms. In 68%, the neck was wider than the parent artery.

In only six (6%) patients, the aneurysm base was free of originating branches, while the remaining 95 (94%) patients had one or more branches originating from the base. A3As had most often branch origins at their base, in 99% of cases. The CMA was the originating artery in 85%, in 12% the aneurysm was at the bifurcation of an azygos ACA, bihemispheric ACA or triplicated ACA, and in 3% the originating branch was some small artery other than the CMA.

5.2.4. Multiple aneurysms

Multiple aneurysms in general were present in 50 (50%) patients including seven (7%) with multiple DACA aneurysms. The distribution of the associated aneurysms is presented in Table 11. The most frequent site for associated aneurysms was the MCA bifurcation with 42 (38%) of the 111 associated aneurysms, a typical finding in a Finnish population with a higher prevalence of MCA aneurysms than elsewhere [49,329].

Table 11. *Distribution of 111 associated aneurysms in 50 patients with multiple aneurysms.*

Location	Number of aneurysms (%)
ICA	16 (14%)
ACoA	11 (10%)
MCA	67 (60%)
VBA	10 (9%)
DACA	7 (6%)

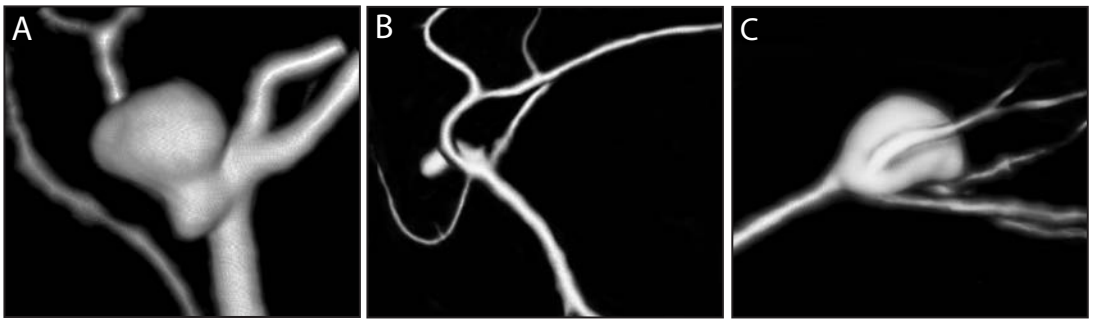


Fig. 15. *(**A**) Anterior A3 aneurysm proximal to the main bifurcation of bihemispheric ACA; (**B**) Anterior A3 aneurysm at the main bifurcation of azygos ACA with three branches at the base; (**C**) A4 aneurysm at the bifurcation of triplicated ACA with three braches originating at the base.*

5.2.5. Anomalies of ACA

A normal course of A2 segments, showing two arteries of similar size running parallel, was observed in 78 (77%) patients (Fig. 3a). The remaining 23 (23%) patients presented various anomalies of the A2 segment (Table 12).

Table 12. *Anomalies of the anterior cerebral artery (ACA) in the 101 patients with DACA aneurysms.*

Type of ACA	No. (%)
Normal anatomy	78 (77%)
Anomalies	23 (23%)
Azygos ACA	4 (4%)
Bihemispheric ACA	15 (15%)
Triplication of ACA	4 (4%)

5.2.5.1. Azygos ACA

A true azygos ACA (Fig. 3b) was present in four (4%) patients. In all of these four patients the DACA aneurysm was located anterior to the genu at the bifurcation of the azygos pericallosal artery.

Fig. 16. *AVM associated with DACA aneurysm (black arrow); the main feeder is the pericallosal artery (white arrow).*

5.2.5.2. Bihemispheric ACA

A bihemispheric ACA (Fig. 3c), the most frequent anomaly of the A2 segment, was seen in 15 (15%) patients. Unlike with the azygos ACA, aneurysms associated with a bihemispheric ACA were not always found at this bifurcation. Only nine (60%) of the 15 patients had their DACA aneurysm at the main bifurcation of the bihemispheric ACA (Fig. 15b), the other six (40%) were either proximal or distal to this point (Fig. 15a).

5.2.5.3. Triplication of ACA

Triplication of the ACA (Fig. 3d) was seen in four (4%) patients. In all four patients, it was the third artery in the midline which harbored

the DACA aneurysm. This artery ran along the corpus callosum and divided into the left and right branches at the aneurysm (Fig. 15c). Two of the aneurysms were located at the A3 segment and two at the A4 segment, more distally than for the azygos ACA.

5.2.6. Associated AVMs

We had only one (1%) patient with DACA aneurysm and associated AVM among the 101 patients (Fig. 16).

5.3. SAH from ruptured DACA aneurysm (publication II, part b)

5.3.1. Age, presentation, and clinical condition

There were 277 patients with primary SAH from a ruptured DACA aneurysm. They were compared to the 2243 consecutive patients with primary SAH from an aneurysm of any location in Table 13. In both series, women somewhat predominated and men bled somewhat earlier. There was a similar initial rebleeding rate in both genders. The more frequent ICHs from ruptured DACA aneurysms did not correlate with the Hunt and Hess grades on admission in either of the two groups (Table 13).

5.3.2. Radiological features

5.3.2.1. CT findings

The ruptured DACA aneurysms presented very often with ICH on the initial CT scan (Fig. 10a), in as many as 53% of them, but there were no differences in IVH or severe preoperative hydrocephalus rates when compared to ruptured aneurysms in other locations (Table 13).

Table 13. *Characteristics and comparison of findings in (1) 277 ruptured DACA aneurysms and (2) all consecutive, ruptured aneurysms in the Kuopio Cerebral Aneurysm Data Base (n=2243) among patients admitted between 1980–2005.*

	DACA aneurysms	All aneurysms
No. of patients	277	2243
Single aneurysm	181 (65%)	1840 (82%)
Multiple aneurysms	96 (35%)	403 (18%)
Sex		
Male	110 (40%)	1059 (47%)
Female	167 (60%)	1184 (53%)
Age [years]; mean (range)	51 (14–80)	51 (5–95)
Male	48 (14–75)	48 (10–86)
Female	53 (30–80)	54 (5–95)
Re-bleeding before treatment	53 (18%)	380 (17%)
Aneurysm size [mm]; median (range)	6 (2–41)	8 (1–60)
Small aneurysms (<7mm)	142 (51%)	936 (42%)
Blood on initial CT scan		
No scan done	16 (6%)	162 (7%)
Fisher grade 1	9 (3%)	71 (3%)
Fisher grade 2	38 (14%)	503 (22%)
Fisher grade 3	52 (18%)	680 (30%)
Fisher grade 4	162 (58%)	827 (37%)
ICHs and IVHs		
Both ICH and IVH	65 (25%)	242 (12%)
ICH only	72 (28%)	296 (14%)
IVH only	25 (10%)	289 (14%)
Neither ICH or IVH	109 (42%)	1254 (60%)
ICH location		
Frontal	131 (96%)	212 (39%)
Parietal	4 (3%)	4 (1%)
Temporal	2 (1%)	322 (60%)
Subdural hematoma	6 (2%)	21 (1%)
Preoperative hydrocephalus	88 (34%)	913 (44%)
Severe	23 (8%)	178 (9%)
Hunt and Hess grade on admission		
Grade 1	41 (15%)	224 (10%)
Grade 2	91 (33%)	916 (41%)
Grade 3	88 (32%)	600 (27%)
Grade 4	31 (11%)	273 (12%)
Grade 5	26 (9%)	230 (10%)
Treatment type		
Clipping	254 (92%)	1664 (74%)
Coiling	12 (4%)	275 (12%)
Conservative	7 (3%)	235 (10%)
Other microsurgical	4 (1%)	69 (3%)

5.3.2.2. Angiographic findings (DSA, CTA, MRA)

The 277 ruptured DACA aneurysms occurred most frequently (81%) on the A3 segment of the ACA. The A2As were somewhat more often ruptured than the AdistAs. Almost all (98%) ruptured DACA aneurysms were saccular, and there were only three (1%) fusiform aneurysms, one (0.4%) traumatic, and two (0.7%) mycotic ones. The ruptured DACA aneurysms were smaller than ruptured aneurysms elsewhere, with median diameters of 6 mm and 8 mm, respectively (Table 13).

5.4. Treatment and outcome of DACA aneurysms (publication II)

5.4.1. Ruptured DACA aneurysms 1936–1979 (publication II, part a)

There were 74 patients with 79 DACA aneurysms treated at our institutions in Helsinki and Kuopio before the year 1980, and 68 (92%) of these aneurysms were ruptured (Table 14). On admission, most of the patients were relatively young (mean age 40 years) and in good clinical condition. At that time surgery was often postponed (median 19 days from the primary SAH) to allow recovery before surgery. With the surgical mortality of only 1% and the management mortality of 13%, this historical series suggests that the surgery of ruptured DACA aneurysms becomes safer when postponed by weeks – although the overall benefit is reduced by early rebleeds as shown in later studies [278]. It also shows how much the results of surgical series on IAs depend on patient selection and how difficult it is to compare results between different series.

5.4.2. Ruptured DACA aneurysms 1980–2005 (publication II, part b)

Of the 277 ruptured DACA aneurysms, 258 were treated with microneurosurgery, 12 with endovascular coiling, and seven conservatively due to initially poor clinical condition (Table 13).

5.4.2.1. Microneurosurgical clipping

Direct clipping was performed in 254 (98%) patients, proximal occlusion of the parent artery in three (1%) patients, and trapping in one (0.4%) patient. Median time from rupture to surgery was two days (range 5 hrs–105 days). The frontal interhemispheric route was used in the majority of the clipped DACA aneurysms [122], and only very proximal A2 segment an-

Table 14. *Characteristics of 68 patients with ruptured DACA aneurysms treated during 1936–1979.*

Number of patients	68
Sex	
Male	41 (60%)
Female	27 (40%)
Age at diagnosis [years]; mean (range)	40 (4–59)
Time from rupture to treatment [days]; median (range)	19 (0–296)
Aneurysm size [mm]; median (range)	7 (3–50)
Clinical condition on admission	
Hunt&Hess grade 1–2	44 (65%)
Hunt&Hess grade 3–5	24 (35%)
Treatment	
Clipping	52 (76%)
Wrapping	1 (1%)
Proximal occlusion	2 (3%)
Explored only	4 (6%)
Conservative	9 (13%)
Surgical mortality	1 (1%)
Surgical morbidity	8 (12%)
Outcome at 1-year	
Favorable outcome (GOS≥4)	53 (78%)
Dead	9 (13%)

eurysms were clipped using the pterional approach or the lateral supraorbital approach [120]. The average operation time from skin-to-skin was two hours (range 45min–8hours). Postoperative angiography, not routine in the early series, was performed in 189 (73%) of the 258 patients. Total occlusion was seen in 172 (91%) patients, neck remnant in 10 (5%), and partial or total aneurysm filling in seven (4%) after the first surgery (Table 15). Morbidity due to treatment was seen in 38 (15%) patients, in most cases a reversible neurological deficit occurred, such as paresis in the lower extremity. Treatment mortality was 0.4%, as one patient died due to postoperative hematoma and brain infarction. The morbidity and mortality rates of microsurgical treatment were equal with the unruptured DACA aneurysms and ruptured aneurysms in general (Table 15).

5.4.2.2. Coiling

Only 12 of the ruptured DACA aneurysms were primarily coiled, with seven of them totally occluded (Table 15). Four patients underwent re-coiling and finally three of them underwent clipping. There was no treatment-related morbidity or mortality in this subgroup of 12 patients.

Table 15. *Treatment details in five different patient groups treated between 1980 and 2005.*

	Ruptured DACAAs,		Unruptured DACAAs,		All ruptured aneurysms,
			no SAH	acute SAH	
	microsurgery	endovascular	microsurgery	microsurgery	microsurgery
No. of patients	258	12	84	20	1664
Occlusion grade after treatment					
Total occlusion	172 (67%)	7 (58%)	58 (69%)	12 (60%)	708 (43%)
Neck remnant	10 (4%)	3 (25%)	2 (2%)	0	67 (4%)
Part of aneurysm filling	6 (2%)	0	1 (1%)	0	25 (2%)
Whole aneurysm filling	1 (0.4%)	2 (17%)	3 (4%)	1 (5%)	56 (3%)
No angiography control	69 (27%)	0	20 (24%)	7 (35%)	808 (49%)
Ventricular drainage	37 (14%)	1 (8%)	2 (2%)	0	290 (17%)
Permanent shunt	28 (11%)	0	3 (4%)	1 (5%)	199 (12%)
Treatment complications					
Intraoperative rupture	57 (22%)	0	6 (7%)	7 (35%)	445 (27%)
Re-clipping or re-coiling	5 (2%)	4 (33%)	2 (2%)	1 (5%)	42 (3%)
Clipping after failed coiling	—	3 (25%)	—	—	—
Epidural hematoma	0	0	1 (1%)	0	5 (0.3%)
Subdural hematoma	3 (1%)	0	0	1 (5%)	16 (1%)
Postoperative ICH	7 (3%)	0	3 (4%)	2 (10%)	27 (2%)
Meningitis, non-bacterial included	24 (9%)	0	1 (1%)	0	111 (6%)
Superficial wound infection	13 (5%)	0	2 (2%)	0	35 (2%)
Morbidity caused by treatment	38 (15%)	0	10 (12%)	3 (15%)	280 (17%)
Mortality caused by treatment	1 (0.4%)	0	1 (1%)	0	8 (0.5%)
Outcome at 1-year					
Favorable (GOS≥4)	193 (75%)	11 (92%)	79 (94%)	11 (55%)	1291 (78%)
Unfavorable (GOS<4)	65 (25%)	1 (8%)	5 (6%)	9 (45%)	373 (22%)

Table 16. *One year outcome for four patient groups admitted during 1980–2005 and treated both actively or conservatively.*

	Ruptured DACAAs	Unruptured DACAAs		All ruptured aneurysms
		No SAH	Acute SAH	
Number of patients	277	94	56	2243
1-year outcome				
Good recovery	159 (57%)	77 (82%)	29 (52%)	1196 (53%)
Moderate disability	45 (16%)	12 (13%)	6 (11%)	352 (16%)
Severe disability	34 (12%)	4 (4%)	4 (7%)	146 (7%)
Vegetative	2 (1%)	0	0	4 (0.1%)
Dead	37 (13%)	1 (1%)	17 (30%)	543 (24%)
Cause of death at 1-year				
SAH related	35 (94%)	0	14 (82%)	500 (92%)
Treatment related	1 (3%)	1 (100%)	0	8 (1%)
Unrelated	1 (3%)	0	3 (18%)	35 (7%)
Management mortality	36 (13%)	1 (1%)	14 (25%)	500 (22%)

5.4.2.3. Outcome at one year

Favorable outcome (GOS 4 or 5) at one year after primary SAH from a ruptured aneurysm was seen in 74% of the 277 DACA patients as compared to 69% of the 2243 patients with ruptured aneurysms of all sites in the Kuopio Cerebral Aneurysm Database (Table 16). The case-fatality rates at one year were 13% and 24%, respectively, and most of the early deaths were directly related to SAH or its sequelae (Table 16).

5.4.2.4. Factors predicting outcome at one year

Risk factors predicting unfavorable outcome (GOS<4) at one year follow-up for the ruptured DACA aneurysms, based on multivariate analysis, were the following: age, Hunt and Hess grade ≥3 on admission, rebleeding before treatment, ICH, IVH, and severe preoperative hydrocephalus (Table 17). Other risk factors did not show statistical significance in the final multivariate model.

Table 17. *Risk factors for unfavorable outcome (GOS < 4) at one year follow-up in 277 patients with ruptured DACA aneurysm during 1980–2005.*

Factor	Univariate Analysis OR (95% CI)	Multivariate Analysis OR (95% CI)
Patient Age (per one year of age)	1.04 (1.02–1.07)§	1.07 (1.04–1.11)§
H&H grade ≥3 on admission	6.46 (3.34–12.52)§	3.90 (1.63–9.34)§
Re-bleeding before treatment	1.59 (0.83–3.03)‡	3.72 (1.50–9.24)§
ICH on pre-op CT	4.91 (2.60–9.31)§	2.74 (1.27–5.92)§
IVH on pre-op CT	5.13 (2.88–9.13)§	2.89 (1.36–6.13)§
Severe pre-op hydrocephalus	13.52 (4.78–38.24)§	6.18 (1.92–19.94)§

In multivariate analysis, odds ratios (ORs) were also adjusted for sex
§ P≤0.01

‡P>0.05

5.4.3. Unruptured DACA aneurysms 1980–2005 (publication II, part b)

5.4.3.1. Unruptured DACA aneurysms without acute SAH

Of the 94 patients with 104 unruptured DACA aneurysms, 57 had no history of prior SAH and 37 had SAH from another aneurysm followed by a good recovery. Of these 94 patients, 84 were treated with microsurgery and three were coiled. Seven patients were treated conservatively because of old age, small aneurysm size (≤2mm) or some other reason. The aneurysm occlusion rate of 91% was the same as in the ruptured DACA aneurysms (Table 15). Intraoperative rupture of unruptured DACA aneurysm occurred in only six (7%) patients, much less often than in patients with acute SAH (see below). There were 10 (12%) patients with postoperative morbidity related to surgery, mostly transient neurological deficits. One patient (1%) died due to postoperative hematoma and infarction. Favorable outcome (GOS 4 or 5) was observed in 95% of the 84 microsurgically treated patients (Table 15). There was no difference in outcome between patients with no history of SAH and those with a history of previous SAH.

5.4.3.2. Unruptured DACA aneurysms with acute SAH

There were 56 patients presenting with unruptured DACA aneurysm(s) in conjunction with acute SAH from another aneurysm. Only 20 (36%) of these 56 patients had their unruptured DACA aneurysms treated, all microneurosurgically in the same session as the ruptured aneurysm through additional craniotomy or exposure (Table 15). The two most important reasons for conservative treatment were small DACA aneurysm size (≤2mm) in 16 patients and poor condition or death in 12 patients. Clipping of unruptured DACA aneurysms in SAH patients was associated with postoperative deficit in three (15%) patients but with no mortality. The incidence of intraoperative rupture was as high as 35% among the 20 unruptured DACA aneurysms treated in patients with SAH from another aneurysm (see above). Outcome at one year follow-up was similar to outcome for other ruptured aneurysms according to Kuopio Cerebral Aneurysm Database (Table 16).

5.5. Long-term follow-up of ruptured DACA aneurysms (publication III)

5.5.1. Rebleeding

A new episode of SAH occurred in four (95%CI 1.09–10.2) of the 280 patients during the follow-up period: (1) rebleeding from a subtotally clipped DACA aneurysm at 17 years; (2) rupture of a de novo MCA aneurysm at two years; (3) rupture of an untreated MCA aneurysm at three years; and (4) rupture of a previously undiagnosed basilar bifurcation aneurysm at five years. The estimated cumulative risk for a new episode of SAH at 10 years was 1.4% (95%CI 0.0–3.0%) and at 20 years 3.0% (95%CI 0.0–6.5%). The incidence for recurrent SAH was 138 per 100 000 follow-up years (95%CI 38–354), which indicates a risk ratio of 3.9 (95%CI 1.5–7.3) compared to the general adult Finnish population with an annual incidence of SAH 35/100 000 [348].

5.5.2. Mortality

5.5.2.1. Early mortality

By the end of follow-up, 92 (33%) of the 280 patients had died, including 36 patients who died within 12 months, implying a 13% management mortality at one year. The causes of these 36 deaths were mostly due to the primary SAH in 33 (92%) patients (Table 18). It is also

noteworthy that 17 (47%) of these 36 patients who died during the first 12 postoperative months were initially in Hunt and Hess groups 4 and 5.

5.5.2.2. Long-term mortality

No patients died of recurrent SAH from a treated DACA aneurysm. One patient died due to SAH from a previously undiagnosed basilar bifurcation aneurysm. Of the 208 patients who had survived more than four years, 42 (20%) died, with cardiovascular disease as death cause in 24% and cancer in 19%. Of the 137 patients who survived for more than 10 years, 24 (18%) died, with cardiovascular disease as death cause in 29% and cancer in 25% (Table 18).

5.5.3. Excess mortality

The 3-year cumulative relative survival ratio (CRSR) was 0.84 (95%CI 0.78–0.88) implying 16% excess mortality for patients with ruptured DACA aneurysm during the first three years after diagnosis when compared with the general Finnish population (Fig. 17). At the fourth year of follow-up, the annual RSR attained 1.0 indicating no excess mortality thereafter (Fig. 18). A separate analysis of the patient group with good recovery at one year showed no excess mortality during the whole follow-up period. The three-year CRSR for women was 0.82 (95%CI 0.74–0.87) and for men 0.86 (95%CI 0.78–0.92) indicating 18% and 14% excess

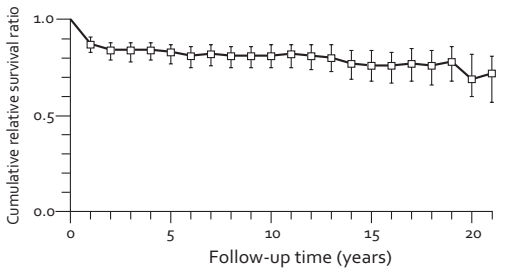


Fig. 17. *Cumulative relative survival ratio (CRSR) of patients with ruptured DACA aneurysm (n=280) as a function of follow-up time in years. Error bars indicate 95% CI.*

Table 18. *Causes of death of the 92 patients who died during the long-term follow-up of 280 patients with ruptured DACA aneurysm.*

	Age at SAH diagnosis	Time of death from diagnosis				Total
	mean±SD	<12mths n	1–3yrs n	4–10yrs n	>10yrs n	n
Related to primary SAH	54±14	33	3	5	2	43
Re-bleeding from treated aneurysm	—	0	0	0	0	0
SAH from another aneurysm	46	0	0	1	0	1
Cerebrovascular	58±12	0	2	1	0	3
Cardiovascular	52±11	1	5	3	7	16
Cancer	55±7	0	0	2	6	8
Infection/Pneumonia	58±11	0	0	2	4	6
Trauma	49±12	1	1	1	1	4
Suicide	48±18	0	1	1	0	2
Other	52±15	1	2	2	3	8
Not known	72	0	0	0	1	1
All deaths	54±13	36	14	18	24	92

n = number of patients
SD = standard deviation

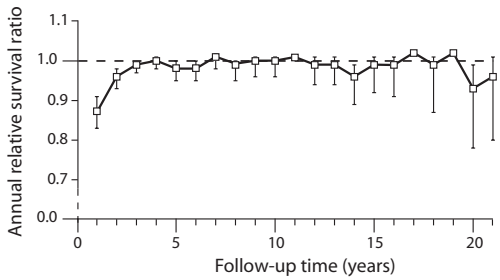


Fig. 18. *Annual relative survival ratio of patients with ruptured DACA aneurysm (n=280) as a function of follow-up time in years. Error bars indicate 95% CI.*

mortality during the first three years, respectively. Analysis by age at diagnosis (<45 years, 45-60 years, >60 years) showed that the youngest group reached the annual RSR=1.0 one to two years earlier with a lower excess mortality in general.

5.6. Microneurosurgical technique for clipping DACA aneurysms (publications IV–VI)

5.6.1. Approach

The DACA aneurysms are generally approached through the anterior interhemispheric approach [441,443]. The only exceptions are some proximal A2As, which may require lateral supraorbital approach (LSO) or pterional approach (see section 5.6.12.1.), but here the vertical distance of 1.5 cm from the anterior skull base to the aneurysm is the limit. Through the interhemispheric approach the exposure depends on the course of the pericallosal arteries, the location of the aneurysm in relation to the GCC, projection of the dome, and possible ICH. For a right-handed neurosurgeon the right-sided approach is more convenient because both of the pericallosal arteries can be reached under the inferior margin of the falx for most of their course. A left-sided ICH or a left-sided associated anterior circulation aneurysm may require a left-sided approach. Importantly, the more proximal the DACA aneurysm lies, the more anterior the approach has to be planned (Fig. 19). With a wrong angle of approach the genu will obstruct the neurosurgeon's view towards the aneurysm base and prevent proper clip placement. We measure the position of the DACA aneurysm in relation to the outside cranium for the exact head positioning and bone flap placement. Usually the shortest route is selected. Some authors have used the bifrontal basal anterior interhemispheric approach [32,390]. We feel that the unilateral approach is less invasive and quicker, and provides equal exposure to the DACA aneurysms deep in the interhemispheric fissure. The technique of clipping ruptured or unruptured DACA aneurysms is almost the same. The only real difference is the lack of working space in acute SAH which makes the whole procedure more difficult. Neuronavigation may be of help in planning and executing the approach towards the aneurysm.

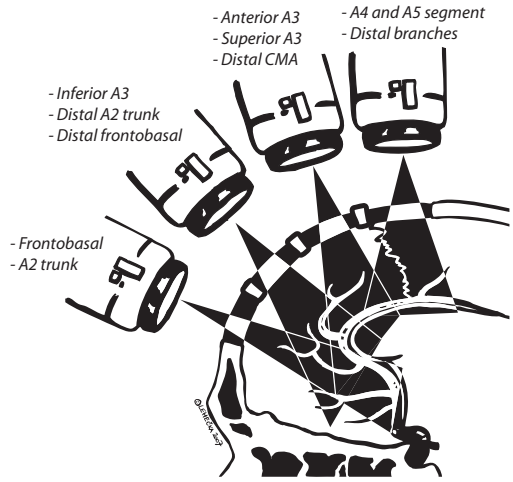


Fig. 19. *Positioning of bone flap during interhemispheric approach for DACA aneurysms at different locations.*

5.6.2. Positioning, craniotomy and dural opening

For the anterior interhemispheric approach the patient is in supine position with the head fixed in a head frame and elevated about 20° above the heart level. The head should be in neutral position with the nose pointing exactly upwards. Tilting the head to either side increases the chance that the bone flap is placed too laterally from the midline. This would make the entrance into the interhemispheric fissure and navigation more difficult. The head is slightly flexed or extended according to how proximal or distal the DACA aneurysm lies. In the optimal position the trajectory is almost vertical. If intraoperative DSA is considered, the frame pins should be placed accordingly or a carbon frame should be used for better visibility. It is our practice to adjust the position of the fixed head and body during the operation when needed [121].

After minimal shaving, an oblique skin incision with its base frontally is made just behind the hairline, over the midline, extending more to the side of the planned bone flap (see DACA — video 1). For some posterior approaches to AdistAs, a straight incision along the midline can be used. Location, curvature, and extent of skin incision depends on the hairline, dimensions of the frontal sinuses, and the orientation of the aneurysm. A one-layer skin flap is reflected frontally with spring hooks. Bicoronal skin incision is unnecessary since strong retraction with hooks often allows anterior enough exposure of the frontal bone. The bone flap is placed slightly over the midline to allow better retraction of the falx medially. The superior sagittal sinus may deviate laterally from the sagittal suture, more often to the right, and as far as 11 mm [410]. The size of the bone flap depends both on the surgeon's experience and on the presence of ICH. We usually use a 3–4 cm diameter flap. Too small a flap may not provide sufficient space for working between the bridging veins. In most patients, only one burr hole in the midline over the superior sagittal sinus at the posterior border of the bone flap is needed. Through this hole, bone can be detached from the underlying dura. One has to be careful with the underlying sagittal sinus, particularly in the elderly with a very adherent dura. The bone flap is removed using a side-cutting drill. High speed drill can be used to smoothen the edges or to enlarge the opening if necessary. If the frontal sinuses are accidentally opened during the craniotomy, they should be packed and isolated with fat or muscle grafts and covered with pericranium.

The dura is opened under the operating microscope as a C-shaped flap with its base at the midline. The incision is first made in the lateral region and then extended towards the midline in the anterior and the posterior direction to prevent opening of the superior sagittal sinus. The dural opening should be planned so that possible meningeal sinuses and lacunae are left intact. Bridging veins may be attached to the dura for several centimeters along the midline. Careful dissection and mobilization of these veins is necessary. It is usually during the opening of the dura that unwelcome damage to the bridging veins takes place. Dural edges are elevated with multiple stitches extended over the craniotomy dressings to prevent epidural oozing into the surgical field.

If the neuronavigation system is used, the correct angle of the trajectory should be verified while planning the skin incision. With the bone flap removed and the dura still intact, the approach trajectory has to be checked again for correct working angle of the microscope. After the dura has been opened and CSF released, brain shift will make neuronavigation less reliable, and one becomes more dependent on the visible anatomic landmarks.

5.6.3. CSF drainage

In case of lateral supraorbital approach (LSO), we release CSF from the supracellar cisterns. In acute SAH, the dissection is then continued from the supracellar cistern subfrontally

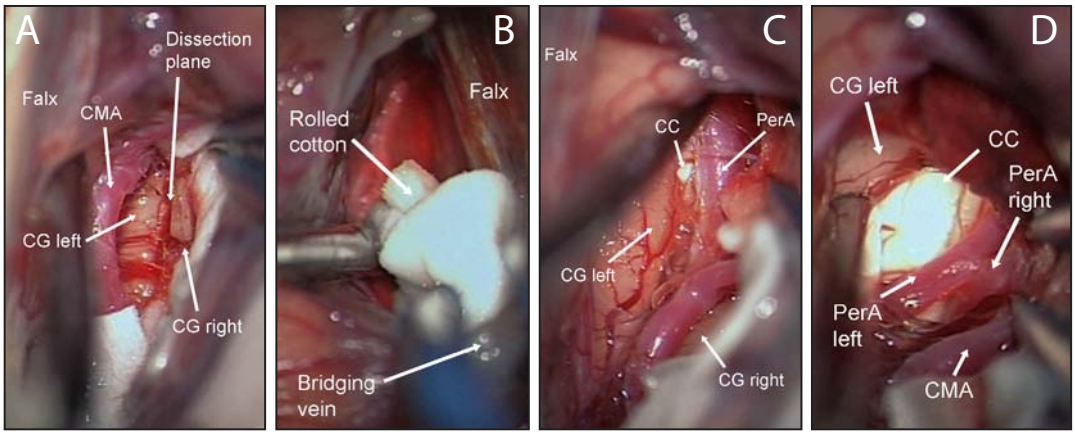


Fig. 20. *Intraoperative photographs of the interhemispheric fissure with (**A**) callosomarginal artery (CMA) and the tightly attached cingulate gyri (CG), (**B**) rolled cottons used as expanders, (**C**) pericallosal artery (PerA) in between the cingulate gyri, and (**D**) white color of the genu of the corpus callosum (CC) (see DACA — video 7).*

towards the optic chiasm and the lamina terminalis which is opened for additional removal of CSF.

The interhemispheric approach provides less space as the callosal cistern is shallow and not much CSF can usually be removed. In unruptured DACA aneurysms, this space will nonetheless usually suffice. In acute SAH, CSF can be released by a puncture to the lateral ventricle at the lateral border of the craniotomy. As an alternative, the corpus callosum can be punctured with a closed bipolar forceps medial to the pericallosal artery, followed by opening of the forceps to create a small channel to the lateral ventricle for CSF release. Partial removal of the ICH may also provide enough space to be able to continue towards the aneurysm.

5.6.4. Removal of ICH

In case of a large ICH and possible lack of space (Fig. 10a-d), a small cortical incision is made accordingly and the hematoma is partially removed to start with to gain more space. This may cause rerupture of the aneurysm which would be difficult to control at this point. In removing the ICH clot, before or after clipping, only minor force should be applied not to sever the perforating arteries. ICH in the immediate vicinity of the aneurysm should be left in place until proximal and distal control have been obtained. In acute SAH, thick blood clots inside the interhemispheric fissure make dissection and visualization of the pericallosal artery and the aneurysm often difficult. Repeated irrigation with saline ("water dissection" [258]) and gentle suction can be used to flush the clots out and to provide better space for further dissection. Only the blood clots which obstruct the approach trajectory are removed. Too extensive removal can easily damage the surrounding brain tissue.

5.6.5. Dissection towards the aneurysm

For the interhemispheric approach, the images should be evaluated for several microsurgical aspects: depth of the falx; depth of the corpus callosum; depth and course of the pericallosal and the callosomarginal arteries; correct parent artery; location of the aneurysm with respect to the GCC (inferior, anterior, superior); size, orientation, and origin of the dome; and possible dislocations due to ICH. CTA should be carefully reviewed for calcifications in the arteries and the aneurysm wall. Calcified plaques in

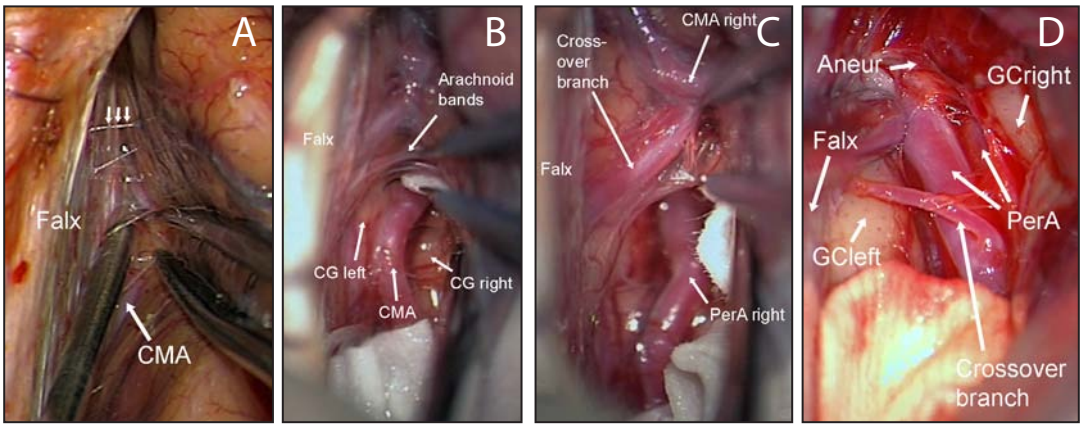


Fig. 21. *Intraoperative photographs of the interhemispheric fissure showing (**A**) the arachnoid bands (small arrows) attached to the falx and the callosomarginal artery (CMA) in the cingulate sulcus, (**B**) the tightly attached cingulate gyri (CG left, CG right) and the CMA running on top of them, (**C**) a large cross-over branch originating form the right CMA, and (**D**) pericallosal arteries (PerA) running parallel with ruptured AdistA surrounded by fresh blood clots and embedded in the right cingulate gyrus (CG right).*

the parent artery will affect temporary clipping, and those at the dome risk intraoperative rupture and incomplete closure of the neck or even complete closure of the parent artery.

We use a hand held syringe to expose and to expand planes for further dissection, i.e., the water dissection technique of Toth [258]. Arachnoid membranes and strands are cut sharply by microscissors which can be also used as dissector when the tips are closed. Use of retractors is kept at minimum, and they are not routinely used at the beginning of the approach. Instead, bipolar forceps in the right hand and suction in the left, with cottonoids of different sizes as expanders, are used as microretractors [121]. When the interhemispheric fissure is widely opened and the frontal lobe mobilized, the retractor may be used to retain some space for clipping, but should otherwise be avoided. Rolled cottons, placed inside the interhemispheric fissure at the anterior and the posterior margin of the approach, provide a more gentle retraction than classical, mechanical retractors (Fig. 20b).

Upon entering the interhemispheric fissure, bridging veins may obstruct the view, preventing even the slightest retraction of the frontal lobe. The veins are likely to restrict the working space and one may have to work between them. It may be of help to dissect some of them for a few centimeters from the brain surface. One may have to sacrifice a smaller vein, with the risk of venous infarction though. Extensive and long-lasting use of retractors, preventing the subsequent venous flow, may have the same result as severing the bridging veins.

Inside the interhemispheric fissure, after clearing the arachnoid adhesions (Fig. 21a), dissection is directed along the falx towards the corpus callosum (see DACA — video 4). The exact orientation of the approach trajectory depends on the location of the aneurysm with respect to the GCC. It is important to be aware of the microscope's angle and the exact head position. With a wrong angle of approach one gets easily lost inside the interhemispheric fissure with no good landmarks to guide towards the aneurysm. At the inferior border of the falx, the dissection plane is identified between the tightly attached cingulate gyri (Fig. 20a, 21b). The pericallosal artery may be found already in the cingulate sulcus, but in most cases the dissection must be continued deeper toward the corpus callosum (Fig. 20c), identified by

its white color and parallel, transverse fibers (Fig. 20d). Falsely assuming the attached cingulate gyri as the corpus callosum, or other paired arteries as the pericallosal arteries, leads to serious problems in navigation.

Once inside the callosal cistern, both pericallosal arteries are visualized, often with a realization that they can be on either side of the midline. The artery leading to the aneurysm is identified and followed to the proximal direction towards the aneurysm. A tedious and careful dissection is performed in the deep and narrow proximal interhemispheric fissure (Fig. 22b). The aim is to identify the proximal part of the parent artery. Landmarks of help are the origin of the callosomarginal artery (Fig. 22a), the genu of the corpus callosum, and possible vascular anomalies recognized in the images (Fig. 23a,b). Since the aneurysm is approached along the distal parent artery, the dome with its possible rupture site is likely to get in the way so as to hide the view to the proximal parent artery, i.e. the site for temporary clipping. Premature rupture at this phase, with little space and no proximal control, may cause great difficulties.

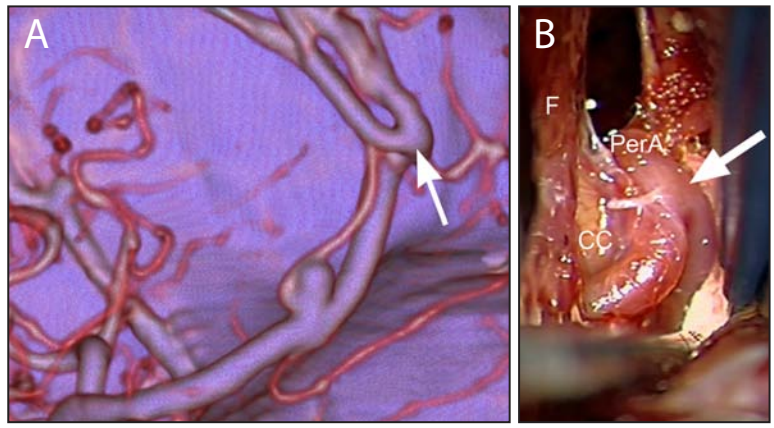


Fig. 23. *(**A**) Azygos ACA with A2 trunk aneurysm as seen on CTA. (**B**) Intraoperative picture of the same patient during anterior interhemispheric approach showing the azygos ACA (PerA) with the bifurcation (arrow), the falx (F) and the corpus callosum (CC) (see DACA — video 4).*

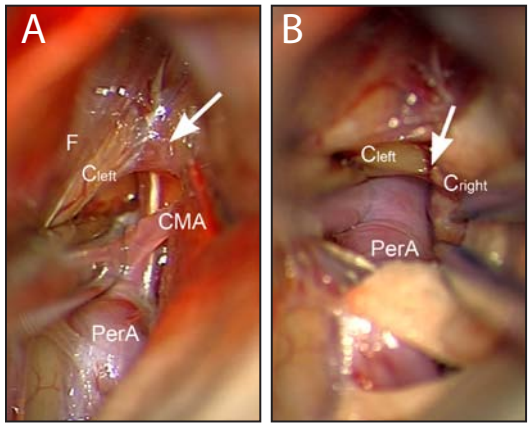


Fig. 22. *Intraoperative photographs demonstrating the narrow interhemispheric space at the (**A**) A3 segment, and (**B**) A2 segment of the ACA. The pericallosal artery (PerA) is running between the strongly attached cingulate gyri (C left, C right) below the lower margin of the falx (F) with dissection plane marked by arrows. The callosomarginal artery (CMA) originates from the A3 segment.*

The dome often extends more to one side and is embedded in the pial layer of the cingulate gyrus (Fig. 21d). This may allow traversing along the opposite gyrus to get proximal control of the parent artery, which is often the most difficult part of the interhemispheric approach. The direction of the aneurysm may change due to retraction and blood may obscure the anatomy, making identification of the aneurysm difficult. Strong retraction is also likely to cause intraoperative rupture. We do not use partial callosal resection to enlarge exposure in the infracallosal region [54]. However, with appropriate head positioning and a well placed bone flap, it is possible to obtain adequate visualization of the aneurysm base without any callosal resection [181].

5.6.6. Dissection of the aneurysm

Small size, thin wall, and a relatively broad base involving branches make the dissection of the DACA aneurysm challenging in the narrow interhemispheric space. The proximal and distal parts of parent arteries as well as all the adjacent branches should be unhurriedly and painstakingly visualized before the final clipping (Fig. 21c). A small subpial resection is often necessary to allow the mobilization and visualization of the whole aneurysm dome.

In acute SAH the cingulate gyri are usually very tightly attached to each other (see DACA — video 9). Dissection of the proximal parent artery can cause great difficulties and it can easily damage both cingulate gyri (Fig. 21d). In such situations, at the expense of poor proximal control, the aneurysm is approached directly and a pilot clip is placed at the neck as soon as possible. With the pilot clip in place dissection of the dome is continued.

5.6.7. Temporary clipping

Temporary clipping facilitates sharp dissection of the aneurysm and the adjacent arteries. Dissection and preparation of the site for the temporary clip(s) should be performed with a blunt-tipped bipolar forceps or with a microdissector. One temporary clip, usually a small one, curved or straight, is applied proximal to the aneurysm (see DACA — video 8). The proximal clip can be close to the aneurysm but the distal ones should be at a distance not to interfere with the visualization and the permanent clipping of the aneurysm neck. In ruptured cases, CMA may require its own temporary clip. When the main part of the base is dissected, a short, straight pilot clip is applied and the temporary clip is removed. When removed, the temporary clip should be first opened carefully in place to test if any unwanted bleeding occurs. Removal in rush can be followed by heavy bleeding and great difficulties in replacing the clip. Furthermore, while removing the temporary clip, even the slightest resistance should be noted as a possible involvement of a small branch in the clip or its applier. If access to the proximal parent artery cannot be achieved, direct pilot clipping is the only choice, and usually a small microclip is applied to the aneurysm base. Longer clips may involve or kink side branch(es).

5.6.8. Clipping of the aneurysm

A proper selection of clips with different shapes and lengths of blades and applicators suiting the imaging anatomy of the aneurysm should be ready for use. Additionally, a limited selection of final clips is needed for temporary clipping of the arteries and bipolar reshaping of the aneurysm dome. DACA aneurysms are generally small with many surrounding small branches. To prevent kinking or occlusion of adjacent branches, the smallest but adequate final clip should be selected. If bipolar reshaping is not considered, the blade of a single occluding clip should be 1.5 times the width of the base. We prefer inserting first a pilot clip to the aneurysm dome, preferring Sugita clips for their wide opening distance and blunt tips. The pilot clip is later changed for a smaller and lighter final clip, after reshaping of the dome by bipolar coagulation (see DACA — video 6). Adequate dissection, proper clip sizes, and painstaking checking that the clip blades are well placed up to their tips are required to preserve the adjacent branches. If the whole dome is dissected free, it may be dislocated to other side with suction to allow better position for the final clip (see DACA — video 4). If the first clip slides, exposing some of the neck, another clip may be applied proximal to the first one for final closure ('double clipping'). Removal of the retractors and cottonoids may lead to kinking of the parent artery or compression of the perforators by the clip blades or the clip itself. The flow has to be checked once more and papaverine applied to release or prevent local vasospasm with only a transient effect.

5.6.9. Intraoperative aneurysm rupture

The DACA aneurysm may rupture while the neurosurgeon is entering the interhemispheric fissure or dissecting the aneurysm base. The risk is high, since most of the aneurysms are oriented so that their dome is encountered before visualization of the proximal artery. The A2As and inferior A3As are particularly problematic and achieving proximal control may be difficult (Fig. 22b). Control should be first attempted via suction and compressing the bleeding site with cottonoids. We keep a second suction prepared before clipping. Sudden and short hypotension by cardiac arrest, induced by i.v. adenosine, can be used to facilitate quick dissection and application of a pilot clip in case of uncontrolled bleeding [321]. A pilot clip may be inserted to a ruptured secondary pouch if visible. Otherwise, temporary clips are inserted proximally on the parent artery, possibly also on branches such as CMA, to allow dissection of the base and final clipping. A small and thin walled aneurysm may rupture at its neck during dissection. In such a case, reconstruction of the base involving a part of the parent artery in the clip should be attempted under temporary clipping.

5.6.10. Verification of clipping

We routinely use micro-Doppler and intraoperative, noninvasive, indocyanine green (ICG) infrared angiography to check the patency of the proximal and distal arteries and branches [315,316], but unexpected occlusions are sometimes seen in postoperative angiography even in very experienced hands [191]. The ICG helps the orientation during dissection, and it visualizes wall thickness and plaques, perforating arteries, and incomplete neck occlusion. ICG angiography reduces the need for invasive intraoperative angiography for clipping control, but DSA is still required in giant and complex aneurysms. The quality and reliability of postoperative CTA is better when titanium clips are used.

5.6.11. Associated aneurysms

DACA aneurysms are often associated with other aneurysms, in 50% of cases in our series. Associated DACA aneurysms were seen in 7% of the patients. Most DACA aneurysms can be reached under the falx even if they are on the contralateral side of the craniotomy. Therefore, bilateral interhemispheric approach is not necessary. Our strategy is to clip all aneurysms that can be exposed through the same approach, i.e. only DACA aneurysms in case of interhemispheric approach. This may not be advisable if clipping of the ruptured aneurysm is difficult or the brain is swollen due to acute SAH [52,330]. Also, this technique of clipping multiple aneurysms simultaneously at different locations is not recommended during the early learning curve. In acute SAH, if there are problems in clipping the ruptured aneurysm, one should not continue with the unruptured one(s). We do not recommend multiple craniotomies for ruptured cases in the acute phase.

5.6.12. Special considerations for each DACA aneurysm location

5.6.12.1. Frontobasal A2As (publication IV)

A2As located on the frontobasal branches of the A2 segment are very rare (Fig. 24a,b). They are usually saccular and small. We approach them through the LSO or the interhemispheric approach, depending on their distance from the anterior fossa.

When close to the skull base, we use the LSO with the benefit of more familiar anatomic landmarks. The vertical distance of 1.5 cm from the anterior skull base to the aneurysm is the limit. The LSO craniotomy is a more subfrontal and less invasive modification of the pterional approach for the anterior circulation aneurysms (see DACA — video 2)[120]. For the LSO approach, it is important to evaluate the distance between the ACoA complex and the optic chiasm, the courses and lengths of the A1

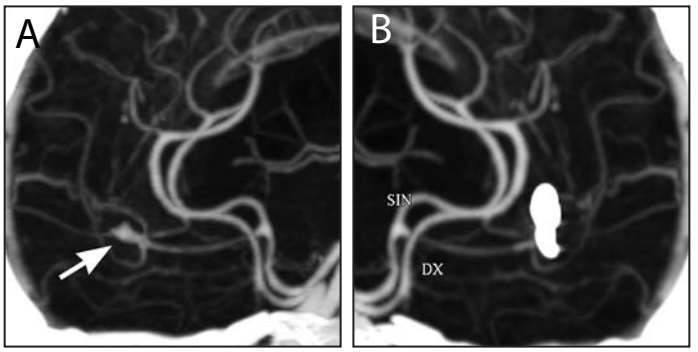


Fig. 24. *Unruptured frontobasal A2A (arrow) at the distal frontopolar artery as seen on (**A**) preoperative and (**B**) postoperative CTA (see DACA— video 5).*

segments, the number and orientation of the A2 segments, the distance of the A2A from the A1–A2 junction, and also the branches in the vicinity of the aneurysm. A small frontobasal resection of the rectal gyrus is usually needed to find the aneurysm. The extent of gyrus rectus resection depends on the distance between the ACoA and the optic chiasm, which can be measured from the images. The RAH and the perforators entering the optic chiasm should not be damaged. The goal is to identify both A1s, the ACoA, and the origins of both A2s.

If the interhemispheric approach is used, the angle of the approach and the distance of the aneurysms from the cranial vault should be evaluated on the images (see DACA — video 5).

A small, straight final clip is usually needed to exclude these aneurysms from the circulation. A neuronavigation system may be of help in finding these aneurysms, but brain shift after CSF release and frontal lobe retraction may be confounding.

5.6.12.2. A2 trunk A2As (publication IV)

A2 trunk aneurysms on the proximal A2 segment can be reached either through the LSO (see DACA — video 3), or the anterior interhemispheric approach. The approach is chosen according to the size and orientation of the aneurysm, its vertical distance from the anterior skull base, possible vascular anomalies, previous surgeries (arachnoid adhesions), rupture status of the aneurysm, projection of the dome, and also the surgeon's preferences. In acute SAH, we prefer the LSO because of (a) the possibility of fenestrating the lamina terminalis, (b) proximal control of the ACoA complex, and (c) easier orientation. The interhemispheric approach, lacking good anatomic landmarks, becomes even more difficult in acute SAH with a swollen brain and also blood clots obstructing the view. A catheter inserted through the fenestration in the lamina terminalis into the

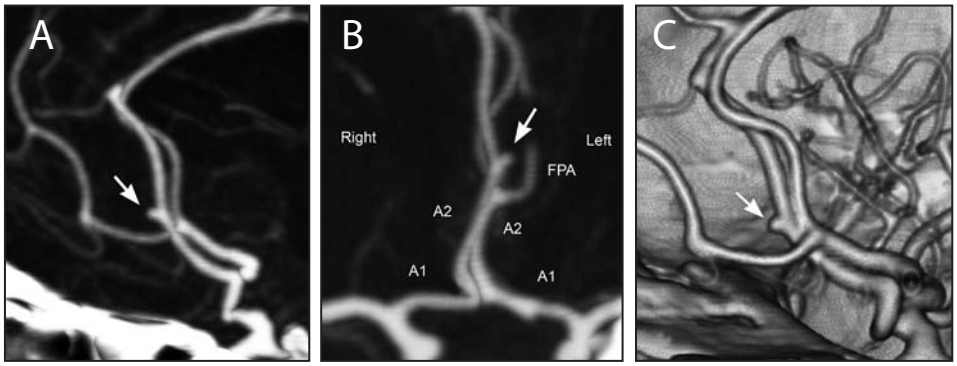


Fig. 25. *CTA images of small, unruptured A2 trunk aneurysm (arrow) as seen on (**A**) sagittal view, (**B**) axial view, (**C**) 3D -reconstruction.*

third ventricle can be left for ICP monitoring and further CSF removal postoperatively.

The anterior interhemispheric approach is used for more distally located A2 trunk aneurysms (Fig. 25a-c) (see DACA — video 4). The gap between the cingulate gyri is deep and narrow, with possible strong adhesions (Fig. 22b). Blood clots and brain swelling in acute SAH make this approach even more demanding. The exposure of the pericallosal artery and the aneurysm depends on the course of the vessel, its location in relation to the corpus callosum, projection of the dome, and an associated ICH.

The main difficulty is to localize the A2 trunk aneurysm, regardless of the approach. Intraoperative DSA may improve navigation during the interhemispheric approach, but in the LSO, the oblique head position is a limiting factor. The neuronavigation system may help early navigation before CSF removal and frontal lobe mobilization.

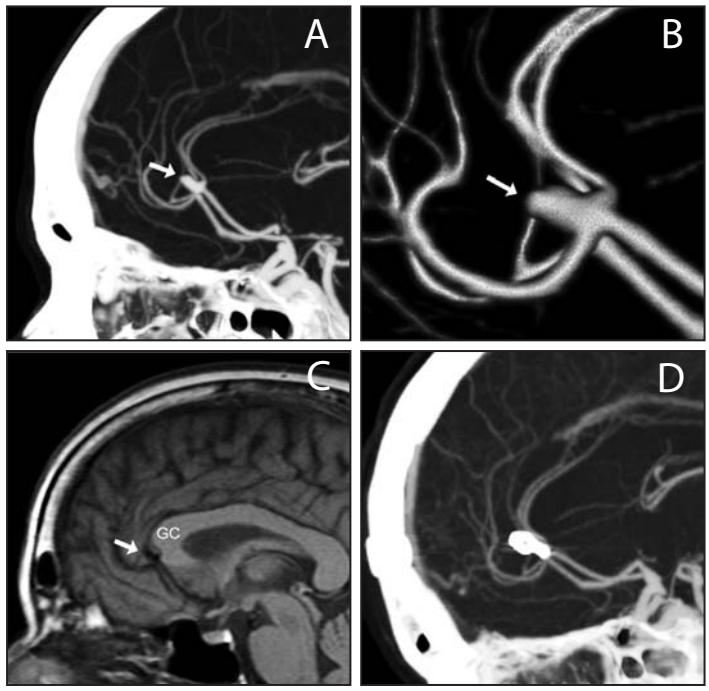


Fig. 26. *Unruptured inferior A3A (arrow) as seen on (**A**) preoperative 2D CTA, (**B**) preoperative 3D CTA, (**C**) preoperative MRI, and (**D**) postoperative CTA (see DACA — video 6).*

Proximal control is particularly difficult in this aneurysm location especially through the interhemispheric approach (see DACA — video 4). A small, straight final clip is usually needed to exclude these aneurysms from the circulation. Extreme care should be taken not to involve the RAH in the clip. Distal A2 trunk aneurysms are usually well above the origin of the RAH.

5.6.12.3. Inferior A3As (publication V)

All A3As are approached via the interhemispheric approach. The inferior A3As are located at the junction of the A2 and A3 segments, inferior to the GCC (Fig. 26a-d)(see DACA — video 6, and DACA — video 7). They require more anterior approach than the other A3As so that the genu does not obstruct the view towards the base (Fig. 19). Inferior A3As usually point forward and slightly upward, with a possible deviation to either side. Proximal control is particularly difficult to obtain in the inferior A3As. Due to their deep location and poor proximal control, inferior A3As are usually more difficult to clip than anterior or superior A3As. As a general rule, the more proximal the A3A lies, the more difficult the clipping is going to be as one has to work deeper in a narrower gap.

The bone flap should be placed as anteriorly as possible without opening the frontal sinuses. Inside the interhemispheric fissure, the dissection is directed along the falx towards the anterior margin of the GCC which is the first landmark. The corpus callosum and both A3s are identified and followed along the curved surface of the genu towards the A2–A3 junction where the A3A lies.

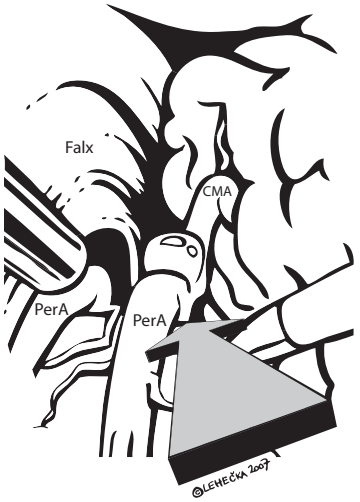


Fig. 27. *Proximal control of the parent pericallosal artery (PerA) can be obtained from below the A3A.*

The parent artery should be visualized if possible, without damaging the cingulate gyri. This may be easier from behind the A3A than in front of it (Fig. 27). If proximal control cannot be obtained, a pilot clip is placed at the dome and under its control the final dissection is carried out. The pilot clip is exchanged for the smallest possible final clip. Care is taken not to occlude branch(es) at the aneurysm base.

5.6.12.4. Anterior A3As (publication V)

The anterior A3As are located at the mid section of the A3 segment, anterior to the GCC (Fig. 28a-d)(see DACA — video 8, and DACA — video 9). The genu does not obstruct the base of the anterior A3As as much as in the inferior A3As, so it is somewhat easier to obtain proximal control. The anterior A3As are usually oriented forward and upward.

A paramedian craniotomy should be placed more posteriorly than for the inferior A3As (Fig. 19). The approach angle should point directly towards the aneurysm. Dissection in the interhemispheric fissure is first directed towards the GCC and, after both A3s have been identified, the appropriate A3 is followed in the proximal direction. The dissection is directed around the aneurysm dome and, if possible, the proximal A3 is exposed.

Final, sharp dissection of the base and the dome is then performed, if possible, with the help of temporary clips. The final clip should be the smallest possible to prevent kinking.

5.6.12.5. Superior A3As (publication V)

The superior A3As, the least frequent of all A3As, are located at the distal part of the A3 segment, superior to the GCC (Fig. 29a-d). The genu does not obstruct the approach trajectory and the parent proximal A3 can be usually visualized for temporary control. Superior A3As are often directed upwards, even backwards.

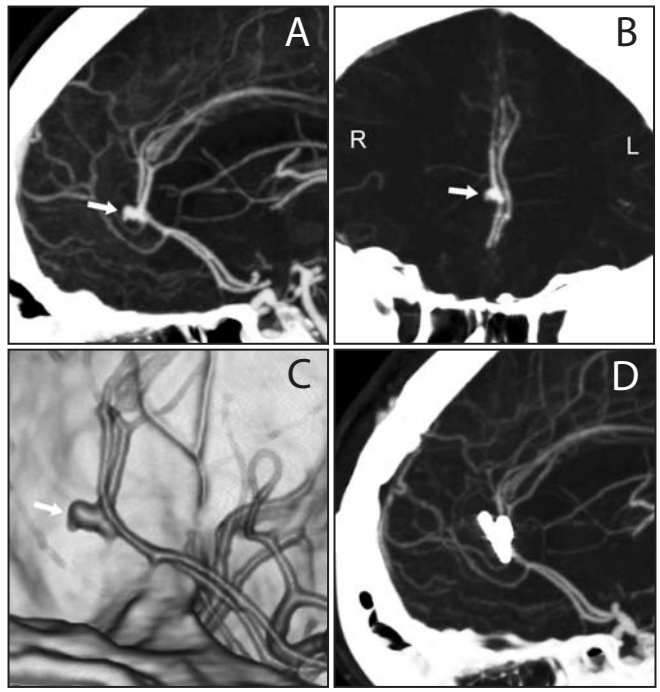


Fig. 28. *Ruptured anterior A3A (arrow) as seen on (**A**) preoperative sagittal CTA, (**B**) preoperative coronal CTA, (**C**) preoperative 3D CTA, and (**D**) postoperative CTA.*

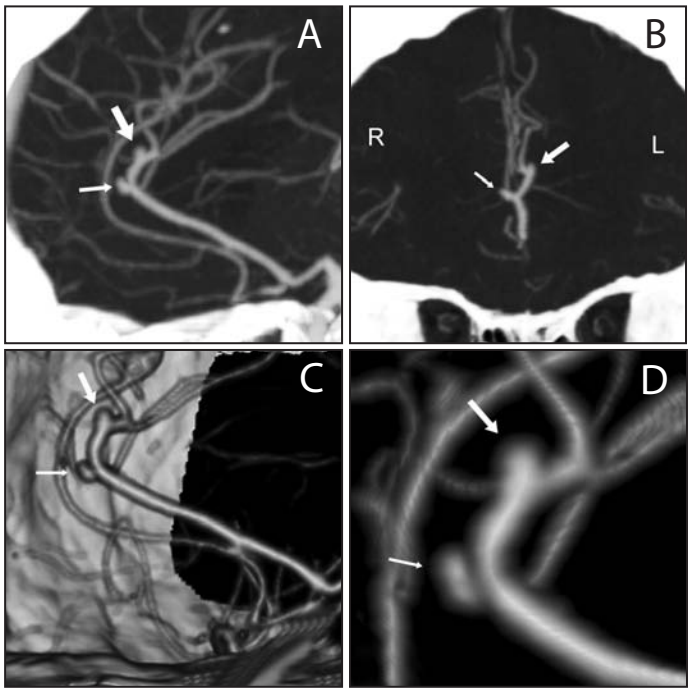


Fig. 29. *Unruptured anterior A3A (small arrow) and unruptured superior A3A found on the same pericallosal artery as seen on CTA in (**A**) sagittal view, (**B**) coronal view, (**C** and **D**) 3D reconstructions.*

The craniotomy is almost the same as in the anterior A3As. The approach angle should point directly towards the aneurysm.

Dissection in the interhemispheric fissure is directed towards the corpus callosum, which is identified along with both A3s and followed proximally. In superior A3As, it is possible to arrive almost directly at the base of the aneurysm. Exposure of the parent A3 should be easier than in more proximal A3As. Dissection of the aneurysm is continued under proximal control. The final clip should be as short and light as possible to prevent kinking of the arteries.

5.6.12.6. A4 and A5 aneurysms (publication VI)

All the AdistAs are approached via the interhemispheric approach, the correct site of the exposure depending on the anterior-posterior location of the AdistA (see DACA — video 10, and DACA — video 11). The approach for A4 and A5 aneurysms is tailored according to the relation of the aneurysm to the corpus callosum and the lower margin of the falx, course of the pericallosal arteries, projection of the dome, and presence and size of a possible ICH (Fig. 30a-c). The A4 segment and the proximal A5

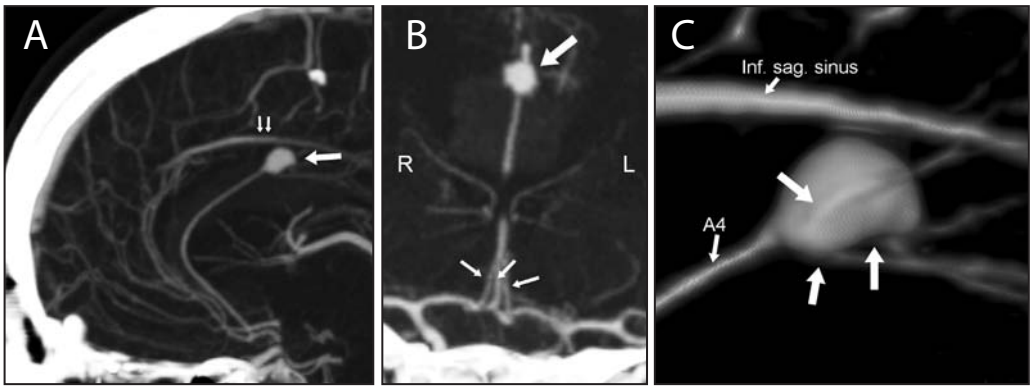


Fig. 30. *Ruptured A4 segment AdistA (large arrow) presenting with ICH (**A**) located below the free margin of the falx and the inferior sagittal sinus (small arrows). Patient has (**B**) triplicated ACA (arrows) with the AdistA on the middle ACA with (**C**) three branches originating from the base (arrows) (see DACA — video 10).*

segment usually lie below the inferior margin of the falx (see DACA — video 10), but the distal A5 segment may be located above it requiring the bone flap on the same side as the aneurysm (see DACA — video 11).

We measure the distance of the aneurysm from the outside cranium, and usually choose the shortest approach. The coronal suture is an excellent intraoperative landmark that should always be identified in the preoperative CT and MRI scans. A4 and A5 aneurysms are very difficult to locate intraoperatively as there are no consistent anatomic landmarks in their vicinity for the orientation inside the interhemispheric fissure. Unlike in the A2As and the A3As, the GCC can no longer be used as an anatomic landmark for orientation. Consequently, the neuronavigator is often helpful in finding the correct angle and approach to the aneurysm.

In AdistAs, distal temporary clipping is seldom needed due to the small caliber of the distal branches. The shortest and lightest possible final clip is used.

5.6.12.7. Distal branch AdistAs (publication VI)

Distal branch AdistAs are located almost always above the free margin of the falx (Fig. 31a-e), which requires the bone flap to be on the same side as the aneurysm, unless the lower portion of the falx is transected. As with A4 and A5 aneurysms, selecting the appropriate approach angle is very difficult and intraoperative identification of the aneurysm may cause great problems due to the lack of proper anatomic landmarks. The neuronavigation system is highly recommended, because these aneurysms are rare and only a few neurosurgeons are used to dealing with them. With a wrong angle of approach one easily gets lost inside the interhemispheric fissure with no good landmarks to guide towards the aneurysm (see DACA — video 12). If possible, we try to approach the distal branch aneurysms along their proximal parent artery to obtain proximal control early in the surgery. Again the shortest and lightest final clip is used.

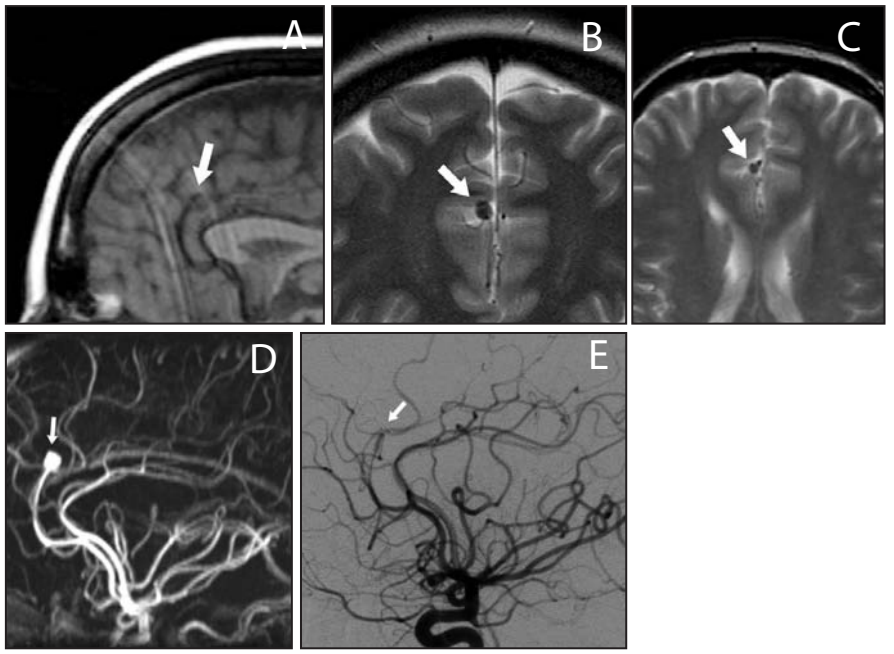


Fig. 31. *Unruptured distal CMA aneurysm (arrow) as seen on preoperative (**A**) sagittal, (**B**) coronal, and (**C**) axial MRI images with the aneurysm in the cingulate sulcus. (**D**) Preoperative MRA and (**E**) postoperative DSA show aneurysm location at the bifurcation of the distal CMA.*

6. Discussion

This series of 517 DACA aneurysms is by far the largest published to date. It is a consecutive series of all DACA aneurysms treated at two Finnish institutions responsible for both primary and secondary care of all SAH patients in their catchment areas. The data are based on an ethnically homogenous population with good medical records and complete follow-up of all patients. The large sample size supports multivariate analysis of prognostic factors. The median follow-up of 10 years provides important data on rebleeding and mortality rates for ruptured and treated DACA aneurysms. Finally, we were able to compare ruptured DACA aneurysms to ruptured aneurysms in other locations in patients with similar characteristics and treatment selection. Results from this study are important when planning microneurosurgical or endovascular treatment of DACA aneurysms.

6.1. Anatomic features

6.1.1. DACA aneurysm locations

Most DACA aneurysms, 69–82% of cases, are found on the A3 segment of the ACA, sometimes called the pericallosal artery–callosomarginal artery junction or "loco classico" [52,122,142,279,312,383,449]. We prefer the term A3 aneurysms, or A3As, since in the present series the CMA was present at the base of these aneurysms in only 84% of the patients. In our material, 84% of all the DACA aneurysms were located at the A3 segment. Of these, 78% were located anterior, 21% inferior, and only 1% superior to the GCC, an important division for microsurgical treatment. The angle of approach has to be selected based on this relationship of the aneurysm with the genu, since with a wrong angle of approach the GCC will obstruct the neurosurgeon's view towards the aneurysm base and prevent proper clipping. For endovascular treatment the distally located aneurysms will be difficult to reach via the small diameter parent arteries and there will be a lack of stability and support for optimal coil deployment.

6.1.2. Aneurysm size and dome orientation

DACA aneurysms are small with the usual size of 5–8 mm [32,52,122,245,264,279,383], in our series 6 mm. Notably, 64% of all the DACA aneurysms and 51% of all the ruptured ones were smaller than 7 mm. Giant DACA aneurysms are extremely rare. The statistical analysis showed no correlation between the size of the ruptured DACA aneurysm and the outcome at one year. Based on our results, at least in the Finnish population with high incidence of SAH [84], the occlusive treatment of unruptured DACA aneurysms smaller than 7 mm is justifiable. For endovascular treatment, the small size of DACA aneurysms, especially those smaller than 3 mm (20% in our material), will make proper coil placement difficult or sometimes impossible.

Most of the DACA aneurysms (93% in our series) have their domes oriented either forwards or upwards. For clipping through the interhemispheric approach this poses a problem, as the dome will initially obstruct the view towards the parent artery. Consequently, controlling the parent artery becomes challenging, especially in cases of intraoperative rupture.

6.1.3. Aneurysm base and associated branches

DACA aneurysms have been observed to have broad bases with possible calcifications and originating branches [122,443]. Our data proved these observations. In 81% of the aneurysms, the neck-to-dome ratio was more than

1:2, with 25% having their neck width equal to the dome width (1:1). At the same time, the neck was wider than the parent artery in 68% of the aneurysms. We identified at least one arterial branch at the base in 94% of the aneurysms. This incidence was even higher for the A3 segment where 99% of aneurysms had branch(es) at their base. All these findings suggest that, irrespective of the treatment modality, it will be challenging to occlude DACA aneurysm completely without compromising the patency of either the parent artery or one of the originating branches. Therefore, clips should be as short as possible, often curved, to prevent accidental occlusion of one of the branches and to avoid kinking of the narrow parent artery. Reshaping of the aneurysm dome with bipolar coagulation before final clipping may sometimes be necessary. Coils need to be well stabilized inside the aneurysm dome to prevent them from migrating into the base and the originating branches.

6.1.4. ACA anomalies

In our series, 23% of the patients had anomalies of the ACA. Bihemispheric ACA, the most frequent one, was seen in 15% of our patients. Azygos ACAs or triplications of ACA were both present in 4%. The azygos ACA was less frequent than what we had expected based on previous reports [32,142,205,383,443]. This is mainly due to the modern DSA and CTA imaging used in this study which allowed better distinction between the different types of anomalies. It is actually very difficult to distinguish a true azygos ACA from the bihemispheric ACA on normal DSA, even with compression of the contralateral carotid artery [14,176]. In patients with triplicated ACA, the aneurysm was found in all cases on the middle artery running along the corpus callosum, also called the hemispheric type of median callosal artery [415]. The only anomalies which could not be clearly observed from our CTA or DSA data were the small cross-over branches from the distal pericallosal artery to the contralateral hemisphere, which should be present in 26–64% of patients [294,380]. This would have required a selective contrast injection into each A2. However, these cross-over branches were frequently observed during surgery (Fig. 21c,d).

Complex bi-, tri-, and quadrifurcations arising from the distal anomalous ACA are thought to contribute to increased blood flow and shear stress on the vessel wall, increasing the susceptibility to aneurysm formation at these locations [10,266]. Of our patients with ACA anomalies, 96% presented the DACA aneurysm on the dominant pericallosal artery. The most typical location was at the bifurcation of this artery in 77%. There were usually two to four branches originating from the base of such an aneurysm and they supplied both hemispheres (Fig. 15a-c). Therefore, in patients with ACA anomalies, damage to the parent artery or occlusion of the branches at the neck will likely result in large, bilateral ischemic areas.

6.1.5. Associated aneurysms and AVMs

A high incidence of associated aneurysms in patients with DACA aneurysms has been reported previously, in 25% to 55% of the patients [52,122,142,279,312,368,376,383,438, 443] . In our series, 52% of the patients had associated aneurysms, much more than the 28–35% reported for other aneurysm locations [49,50,70,140,331]. Statistical analysis in our series did not show any correlation between multiple aneurysms and hypertension, sex or polycystic kidney disease. High incidence of associated aneurysms necessitates careful decision making on how to treat the large number of unruptured associated aneurysms (see section 6.3.2.). AVMs and DACA aneurysms co-existed in our material in only 1% of the patients, much less than the 3–15% described in previous reports [52,383,438]. This could be due to less selected patient population in our centers.

6.1.6. ICHs from ruptured DACA aneurysms

The high incidence of ICHs, small aneurysm size, and high number of associated aneurysms were the special features of the ruptured DACA aneurysms in comparison to the ruptured intracranial aneurysms in general. In previous reports, an ICH was related to a ruptured DACA aneurysm in 17–73% of the cases [122,172,231, 312,368,376,383]. In our series, 53% of patients with a ruptured DACA aneurysm had an ICH on the initial CT scan as compared to 25% for the ruptured aneurysms in general. The high incidence of ICHs is obviously related to the narrow pericallosal cistern and dense attachments of the aneurysm with the adjacent brain. ICHs were relatively well tolerated in patients with ruptured DACA aneurysms as they had a similar distribution of preoperative Hunt and Hess grades compared to patients with ruptured aneurysms in general. Nonetheless, ICH predicted unfavorable outcome in patients with ruptured DACA aneurysms. The presence of an expansive ICH in a ruptured DACA aneurysm favors clipping over coiling but at the same time makes the microneurosurgical approach much more demanding due to the lack of space and distorted anatomy.

6.1.7. Imaging of DACA aneurysms and CTA

Even though DSA has been the gold standard of aneurysm imaging in the past [237], during the last decade CTA has become the primary imaging method in many centers as it is noninvasive, fast, and offers similar resolution in aneurysms larger than 2 mm [165,292]. All previous, larger series on DACA aneurysms have used DSA data for radiological analysis [52,122,312,383]. Our series is the first one which is largely based on CTA data in 61% of the patients. CTA seems to solve certain problems compared to planar DSA images: it gives more accurate information on the aneurysm location with respect to the corpus callosum, and with a possible ICH. In addition, the 2D and 3D reconstructions show the exact dome orientation and base morphology with respect to the originating branches, and they also help to determine from which artery the aneurysm originates. With CTA, it is possible to evaluate all the vessels of the anterior circulation at the same time, which enables more accurate distinction between the different ACA anomalies, better evaluation of the whole ACoA complex, and easier identification of the associated aneurysms. Based on this series, we would strongly recommend either CTA or modern rotational DSA for preoperative imaging of DACA aneurysms.

6.2. Treatment of DACA aneurysms

6.2.1. Clipping of DACA aneurysms

Microsurgical clipping of DACA aneurysms presents certain specific difficulties when compared to other anterior circulation aneurysms [52,122,142,231,248,264,279,312,383,438,443, 445].

Yaşargil listed these special features as [443]:

i) Lack of working space in the interhemispheric space and pericallosal cistern.
ii) Dense adhesions between the cingulate gyri make separation and finding of the aneurysm difficult.
iii) Sclerotic wall and broad base of the aneurysm require precise positioning of the aneurysm clip.
iv) Origins of the branching arteries at the neck and attachment of the dome to the opposite pericallosal artery increase risk of vascular ischemic complications.
v) Difficulty in identifying lateralization of the parent artery from the preoperative images.

vi) Attachment or embedding of the dome in the pial layer of the cingulate gyrus increases risk of tear in the aneurysm wall during dissection.
vii) With aneurysm at the bifurcation of an azygos pericallosal artery, complications may lead to vascular damage of both hemispheres.

Based on our observations, we wish to add the following features:

viii) The bridging veins cause difficulties in entering the interhemispheric fissure.
ix) Frontal expansive ICH results in lack of space and difficult dissection.
x) Frequent intraoperative ruptures occur due to unfavorable angle of approach.
xi) Difficulty in obtaining proximal control, particularly in the region inferior to the corpus callosum.
xii) Small aneurysm size makes correct clip placement difficult.
xiii) Orientation problems in acute SAH with thick blood clots inside the interhemispheric fissure.
xiv) Problems in localizing the aneurysm due to lack of consistent anatomic landmarks.

Despite these challenging features, microsurgical clipping still remains the primary occlusive treatment modality for DACA aneurysms over the present techniques of endovascular therapy. In the present series, the complication rates for microsurgical treatment were similar in the ruptured and unruptured DACA aneurysms, and they did not differ from those of other aneurysm locations.

6.2.2. Coiling of DACA aneurysms

So far, although the published series on endovascular treatment of DACA aneurysms are small, most authors have reported more procedural difficulties than for other aneurysm locations [184,265,291]. In our small series of 12 coiled patients with ruptured DACA aneurysm, the success rate in total occlusions was lower than after microsurgical clipping. Our material is too small to evaluate the long-term clinical outcome after coiling of DACA aneurysms. Even with the present technology, endovascular occlusion of DACA aneurysms is still demanding because of the small size, relatively wide neck, branches originating close to the base, small caliber of parent artery, and distal location of the aneurysm. The high incidence of ICHs in patients with ruptured DACA aneurysms also favors microsurgery for immediate clot removal. In our practice we discuss each aneurysm patient in our neurovascular group and select the treatment modality for each patient individually in order to obtain the best possible overall result in the long run.

6.3. Outcome

6.3.1. Ruptured DACA aneurysms

6.3.1.1. One year outcome

Microsurgical series on patients with ruptured DACA aneurysms have reported favorable outcome in 58–83% and management mortality in 7–21% of the cases, respectively [52,122, 231,264,279,312,368,383,438]. This is well in line with the 74% favorable outcome and 13% case-fatality rate in our material with complete follow-up. The Cooperative Study showed far worse results after conservative treatment of ruptured DACA aneurysms than for any other aneurysm location, with a 75% mortality [267]. Likewise, some surgical series have suspected less favorable prognosis for patients with DACA aneurysms when compared to other aneurysm sites [52,231]. We did not see such a trend in our series.

Based on our results, with modern treatment methods, ruptured DACA aneurysms

carry similar prognosis for favorable outcome as other ruptured aneurysms but their mortality rate is lower. This might be due to the frontal and relatively superficial location of DACA aneurysms. As we have observed, almost all ICHs related to ruptured DACA aneurysms are in the frontal lobes. If similar sized hematomas were located in more central regions of the brain or closer to eloquent areas, their effect on patients' outcome would probably be much more devastating. The same applies to vascular complications, e.g. ischemia related to occlusion of the distal anterior cerebral artery is probably better tolerated than ischemia in central structures. Therefore, patients with ruptured DACA aneurysms will not die of SAH as frequently as patients with other ruptured aneurysms, and they will have equally favorable outcomes as patients with other ruptured aneurysms. However, there will be more of those with severe disability among the survivors.

6.3.1.2. Predictors of outcome at one year

For patients with ruptured DACA aneurysms we found age, Hunt and Hess grade, rebleeding before treatment, ICH, IVH, and severe preoperative hydrocephalus as independent factors predicting unfavorable outcome at one year follow-up. Hunt and Hess grade was the only one of these factors also identified by previous series on DACA aneurysms [248,383]. Similarly, series on other aneurysm locations have observed the effect of the initial grade on patient outcome [287,329,342]. Among the patients with H&H≥3, those with ruptured DACA aneurysms did better at one year than those with other ruptured aneurysms, with favorable outcomes of 59% and 49%, respectively. Based on this finding, one might consider a more active approach towards treatment of poor grade SAH patients when the SAH is caused by a ruptured DACA aneurysm.

Our initial CT findings were strongly related to outcome. ICH, IVH and severe preoperative hydrocephalus all predicted unfavorable outcomes. The combined presence of these three factors was especially devastating. Previously, blood seen on the preoperative CT scan (Fisher grade ≥ 3) has been shown to associate with poor outcome in patients with SAH in general [287,329]. The same seems to apply for ruptured DACA aneurysms in cases where the blood is either intraparenchymal or intraventricular. Blood clots in the subarachnoid space only (Fisher grade = 3) were not associated with outcome in our series.

Although rebleeding was not a statistically significant predictor for outcome in the univariate analysis, the multivariate model revealed it was an independent risk factor. It is also the only risk factor that can be prevented by rapid neurosurgical intervention. It has become our policy to treat patients with ruptured aneurysms as soon as possible, preferably within the first 24 hours and no later than 72 hours after the initial rupture to prevent possible rebleedings [278].

6.3.1.3. Neurological deficits

DACA aneurysms are sometimes associated with certain unique neurological deficits such as akinetic mutism, bilateral leg weakness, behavioral changes and cognitive deficits [33,71,87,99,382]. In our series, we were not able to identify any patients with akinetic mutism or bilateral leg weakness among the patients with favorable outcome. These symptoms were probably present in some of our patients with unfavorable outcome, but may have been masked by the overall poor condition of these patients. Therefore, we were not able to determine the incidence rates of these neurological deficits in our series.

6.3.2. Unruptured DACA aneurysms

Clipping of unruptured DACA aneurysms was a safe and effective method in our series. The most important factor determining the outcome in these patients was the presence

or absence of acute SAH. Clearly, patients in whom the unruptured DACA aneurysm was treated during the acute SAH phase did worse than those treated later on after recovery; the latter group had the same excellent results as patients with no history of SAH. We did not observe a similar difference in patients with SAH caused by a ruptured DACA aneurysm. In these patients, simultaneous treatment of associated DACA aneurysm(s) did not affect the outcome. The same also applied to patients without SAH in whom the treatment of multiple aneurysms had equally favorable outcome. Our results suggest that, in patients with acute SAH, associated unruptured DACA aneurysm(s) should be treated only when they can be reached easily via the same microsurgical approach, i.e. only if the SAH is caused by an other DACA aneurysm. In all other cases one should wait for the patient to recover from the SAH and its primary treatment and then treat the unruptured DACA aneurysm in a separate session together with possible other associated aneurysms.

6.4. Long-term follow-up

6.4.1. Rebleeding from clipped DACA aneurysms

In our series with a median follow-up time of 10 years, there was only one rebleeding (0.4%) at 17 years after the initial clipping and no deaths from the 262 clipped DACA aneurysms. DACA aneurysms are located relatively distally in the cerebrovascular tree with narrow parent arteries, which could indicate a smaller shear stress onto the vessel wall, making DACA aneurysms less prone to rebleeding than aneurysms at more proximal locations [427]. Based on our results microsurgical clipping is a long-lasting treatment for DACA aneurysms.

6.4.2. Recurrent SAH and de novo aneurysms

During the long-term follow-up we observed four new episodes of SAH, but only one from a DACA aneurysm. The cumulative incidence rate for recurrent SAH at 10 years was 1.4%. This was similar to a Japanese study where the risk for SAH from a de novo aneurysm was 1.4% during the 10-year follow-up [409]. Only one of the 92 deaths (1%) was due to recurrent SAH from a de novo or a previously undiagnosed aneurysm. De novo aneurysms have been reported to develop at a 0.84–0.89% annual rate [161,408]. Altogether, recurrent SAH seems to be a rare cause of death during a long-term follow-up in patients after surgically treated ruptured DACA aneurysms, even if the cumulative rupture rate increases with follow-up time and the relative risk compared to the general population is higher [160,419].

6.4.3. Mortality

The management mortality at 12 months was 13%, similar to previous studies [337,338], and most of these early deaths (92%) were directly due to the primary SAH and its sequelae. Later in the follow-up, the distribution of death causes started to resemble that of the general Finnish population with two major causes of death, cardiovascular disease and cancer. Several studies have addressed the acute extracranial complications after SAH such as cardiac arrhythmias, cardiac dysfunction, myocardial injury, pulmonary edema, acute lung injury, and renal or hepatic dysfunction [377,413], but there are no studies on the long-term effect of SAH on the cardiorespiratory system. Hypertension and smoking are important risk factors for SAH but they also predispose to cardiovascular disease and cancer [76,156].

6.4.4. Excess mortality

Relatively little is known about the long-term survival after aneurysmal SAH as only two population based studies have been published [281,337]. Both of these studies used the standardized mortality ratio (SMR) as a measure of excess mortality instead of the annual relative survival ratio (RSR) [69]. Unlike the SMR, which is a quotient of the observed over the expected number of deaths, the RSR takes into account the temporal variation of excess mortality [69]. This makes it a more sophisticated method for evaluation of excess mortality. In our series, the patients who survived three years from rupture of DACA aneurysm experienced no excess mortality compared to the matched population.

6.4.5. Long-term angiographic screening

Based on our study, routine angiographic control studies during a long-term follow-up are unlikely to be effective in preventing new episodes of SAH [161]. Young patients with multiple aneurysms, family history, and heavy smoking may need to be followed up at 5 to 10-year intervals. Our data supports the view that, after a recovery period, ruptured and treated DACA aneurysm should not cause any long-term effects on life expectancy. Aneurysms at other locations may behave differently. At the moment, unfortunately, we do not have such data available which would allow us to perform similar survival analysis for other aneurysm locations.

6.5. Future trends

Intracranial aneurysms are found in about 2% of the population, but the majority of them actually never rupture. Sadly, those that do rupture have a 50% mortality even with the best possible treatment. This indicates that the biggest advance in the treatment of this disease will be obtained by preventing aneurysms from rupturing altogether. Therefore, the future treatment of IAs should focus on several different issues, in many of which progress cannot be made without the data obtained from basic research:

1) *Identification of patients with IAs.* The key to prevent SAH is to identify and treat the individuals harboring IAs before they rupture. Screening with present imaging techniques is too time consuming and expensive to be used on a large scale outside of special groups known to be at high risk for IAs. In the future, once the genetic background of the IA disease is known, it may be possible to effectively identify patients at risk using a simple blood test, and these patients could then be selectively imaged with MRA or other method for possible IAs.

2) *Patients with familial background.* One of the high-risk groups for IAs are individuals who have relatives with IAs. In the near future, the whole genome mutation analysis may provide more insight into the genetic defect behind the high number of IAs in certain families. Identification of the defective genes could provide means to screen more effectively for possible individuals at increased risk of being carriers for IA.

3) *Identification of rupture-prone aneurysms.* Since most aneurysms never rupture, a special method enabling differentiation between stable and rupture-prone IAs is needed. It is evident that the aneurysm size or location is not a very accurate method. We would need better tools to evaluate the aneurysm wall type and to map the possible weak areas of the dome under increased hemodynamic stress. Results of basic research could be utilized for the development of targeted local therapy which would stabilize and reverse the degeneration and inflammation processes in the aneurysm wall.

4) *Targeted pharmaceutical therapy*. Genetic studies focused on finding the gene(s) responsible for IA development should enable development of targeted pharmaceutical therapy to reverse the process. This therapy could then be used either locally to prevent aneurysm formation at defined locations or to prevent IA formation altogether via a systemic route. Development of a pharmacological intervention, if successful, is probably going to be the most important advance in IA treatment.

5) *Preventive treatment of risk factors* (smoking, hypertension, alcohol consumption). Risk factors associated with IAs and SAH are the same as those for cardiovascular diseases in general. Increasing awareness of healthier lifestyles and dietary habits and their relationship with cardiovascular diseases still require plenty of work on the population level.

6) *Endovascular methods.* Endovascular techniques will probably evolve toward exploiting much smaller-diameter, biologically active embolic materials, which will be deployed into the aneurysm with much better precision than offered by the present methods. The bioactive materials will be more durable and also have a therapeutic effect on the vessel wall. Preoperative imaging and flow-models of the various flow zones inside the aneurysm and the whole vascular tree could be used for guiding the embolic material into the proper place. The rapidly evolving nanotechnology may one day allow the neurosurgeon to navigate a tiny robot inside the vessels in order to heal the arterial wall locally. The borderline between endovascular and microneurosurgical treatment is likely to fade, and novel techniques might emerge using both approaches simultaneously.

7) *Microneurosurgical techniques.* The trend in microneurosurgical techniques is towards adoption of increasingly less invasive procedures, which can be performed fast and under local anesthesia. Microscopes are already being equipped with diverse new features enabling better visualization of the operative field and blood flow, but in the future they might also allow observation of the microanatomic structure of the aneurysm wall and identification of the weak areas. Development of smaller, lighter, and more flexible endoscopes with stereoscopic vision will provide new means for planning mini-invasive microsurgical approaches. Simple and fast while preserving the normal anatomy should be the key criteria.

8) *Considerations for the aging population*. The growing demands for active medical treatment in the aging patient population will challenge the protagonists of both endovascular and microneurosurgical treatment. Increasingly older patients with more comorbidities will ask for preventive treatment of their unruptured aneurysms. This will require special mini-invasive and fast treatment approaches not only from neurosurgeons but also from neuroanesthetists. The treatment guidelines will have to be reevaluated as well.

9) *Redo aneurysms.* With the increasing number of unruptured aneurysms being detected and treated, the number of treatment failures and recurrences will also increase. These redo cases of aneurysms filled with embolic material from the previous treatments will pose a special challenge. They will require a combination of endovascular and microsurgical approaches, including bypass surgery, for optimal results. Therefore, specialized neurovascular collaborative teams consisting of neurosurgeons, neuroradiologists, neuroanesthetists, and

neurointerventionalists will be needed to take care of these patients.

7. Conclusions

I. Even when ruptured, DACA aneurysms are small, and often with wide necks and narrow parent artery diameters. Almost all of them have at least one branch originating from the base. DACA aneurysms are usually located on the A3 segment of the ACA, anterior to the genu of the corpus callosum. Anatomic anomalies of the ACA, especially the bihemispheric ACA, are frequently observed in association with DACA aneurysms.

II. Microsurgical clipping is a safe and effective treatment method for DACA aneurysms with similar complication rates as for aneurysms at other locations. Ruptured DACA aneurysms present with similar one-year favorable outcome as ruptured aneurysms elsewhere, but their mortality is lower. Factors predicting unfavorable outcome are advanced age, poor grade on admission, rebleeding before treatment, ICH, IVH, and severe preoperative hydrocephalus. Occlusive treatment of unruptured DACA aneurysms even smaller than 7 mm is justified, especially in Finland, in patients with otherwise good prognosis.

III. After surviving three years from the initial SAH, patients with ruptured DACA aneurysms have similar survival prognosis as the matched general Finnish population. During the first three years, the excess mortality is mainly due to the primary SAH or its sequelae. After three years, the leading causes of death are cardiovascular disease and cancer, as in the general population. Clipping is a long-lasting treatment for DACA aneurysms with a very low rate of rebleeding.

IV.-VI. Modern microneurosurgical management of DACA aneurysms requires detailed knowledge of the microanatomy of the anterior cerebral artery and the surrounding structures. The challenge is to select the appropriate approach, locate the aneurysm deep inside the interhemispheric fissure, and to clip the neck adequately without obstructing the branching arteries at the base. Each DACA aneurysm location requires some modification to the general approach.

List of 12 supplementary videos on microneurosurgery of DACA aneurysms

The supplementary CD includes these 12 videos on microneurosurgery of DACA aneurysms:

1. Craniotomy and exposure for interhemispheric approach (DACA — video 1)
2. Craniotomy and exposure for later supraorbital (LSO) approach (DACA — video 2)
3. Clipping of proximal A2 trunk A2A through LSO (DACA — video 3)
4. Clipping of distal A2 trunk A2A (DACA — video 4)
5. Clipping of distal frontopolar artery A2A (DACA — video 5)
6. Clipping of unruptured inferior A3A (DACA — video 6)
7. Clipping of unruptured inferior A3A (DACA — video 7)
8. Clipping of unruptured anterior A3A (DACA — video 8)
9. Clipping of ruptured anterior A3A (DACA — video 9)
10. Clipping of ruptured A4 segment AdistA (DACA — video 10)
11. Clipping of unruptured A5 segment AdistA (DACA — video 11)
12. Clipping of ruptured distal CMA aneurysm (DACA — video 12)

All the videos are in QuickTime® format and require a QuickTime® player to be installed. The videos were recorded during microneurosurgical operations on DACA aneurysms by Professor Juha Hernesniemi from 2005 to 2007 at the Department of Neurosurgery, Helsinki University Central Hospital, Helsinki, Finland. Professor Hernesniemi has operated on 149 patients with 184 DACA aneurysms since 1981.

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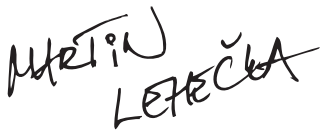

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